

A Dissertation on
OCULAR MANIFESTATIONS OF
HIV/AIDS IN ADULTS
AT THE TIME OF DIAGNOSIS



Dissertation submitted for
M.S. Degree in Ophthalmology
April 2013



THE TAMILNADU Dr. M.G.R. MEDICAL UNIVERSITY

CHENNAI, TAMILNADU

DECLARATION

I hereby declare that this dissertation entitled “**OCULAR MANIFESTATIONS OF HIV/AIDS IN ADULTS AT THE TIME OF DIAGNOSIS**” is a bonafide and genuine research work carried out by me under the guidance of Dr A RAJENDRA PRASAD MS DO, Professor of Ophthalmology, Coimbatore Medical College, Coimbatore.

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Dr B SOWKATH ALI

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The incidence of new HIV infections occurring globally each day is about 14,000 of which more than 95% are in developing countries. The cumulative lifetime risk of developing ocular manifestation in HIV positive person is found to be between 52 to 100 % in various studies.

OBJECTIVES:

1. To define the ocular manifestations of HIV/AIDS in adults at the time of diagnosis.
2. To determine the prevalence of ocular manifestations of HIV/AIDS in adults at the time of diagnosis
3. To correlate the manifestations with the demographic profile and clinical stage of the disease.
4. To determine the visual impairment associated with ocular manifestations.

MATERIALS AND METHODS:

A total of 76 persons who were diagnosed recently as HIV positive and attended the OP clinic of department of STD (sexually transmitted diseases) and ART centre were screened for ophthalmic status with resources provided after getting a clear consent.

Among the 76 persons examined 30 had ocular lesions; of which 26 had HIV related ocular manifestations and 4 had HIV non related ocular manifestation. 12 had posterior segment, 6 had anterior segment lesions, 6 had adnexal lesions, while 2 had Neuro ophthalmological lesions. HIV retinopathy is the most common isolated ocular manifestation found in about 10 persons.

CONCLUSION:

The prevalence of ocular manifestations occurring in adults at the time of diagnosis was 24.34%. No significant association was found with the demographic profile, mode of transmission and concurrent history of tuberculosis. Though, significant association was found with clinical stage of the disease and the concomitant presence of ocular symptoms. The prevalence of visual impairment due to HIV associated ocular manifestation is around 6.57%. Hence, the present study strongly emphasizes the importance of routine ophthalmic screening at the time of diagnosis of HIV seropositivity in adults.

KEYWORDS:

Human immunodeficiency virus, CD4 count, WHO staging, HIV retinopathy, Herpes zoster Ophthalmicus, Visual impairment.

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INTRODUCTION

Human immunodeficiency virus (HIV) is a member of the family Retroviridae, a group of RNA viruses that possess an RNA dependent DNA polymerase known as reverse transcriptase. Three subfamilies of Retroviridae has been reported namely Oncovirinae, Spumavirinae and Lentivirinae, of which HIV is related to lentivirinae.^{1,2} The epidemic of HIV associated disease has been first identified in 1981 and in 1982 the term “AIDS” denoting ***ACQUIRED IMMUNE DEFICIENCY SYNDROME***, the final manifestation of HIV disease has been coined. In 1983, the etiologic agent was identified with the discovery of human T cell lymphotropic virus type III in United States.^{1,3} In India, HIV was first identified in 1986 in Chennai among commercial sex workers. At present the prevalence of HIV infected people in India is 2.5 million and in worldwide it's about 65 million.^{4,5} The incidence of new HIV infections occurring globally each day is about 14,000 of which more than 95% are in developing countries. Eighty percent of the new HIV infections are due to heterosexual transmission and majority occurring in persons aged between 15 to 49 years.^{4,6}

Ophthalmic manifestations are common in HIV infected patients occurring in more than 90% of autopsy cases in one series.¹ The cumulative lifetime risk of developing at least one abnormal ocular lesion for a HIV positive person during the course of the disease is found to be between 52 to 100 % in various studies. Ocular lesions usually occur in the late phase of the disease but can also occur in the early stages also.^{4,7} The first case of AIDS with ocular lesions reported from India had CMV retinitis along with dementia.^{8, 9} Ocular manifestations may be the initial presentation of a systemic infection in an asymptomatic HIV positive patient.^{8, 10} Hence early detection of the manifestations is critical which has got an impact on the prognosis of the disease.^{11,12} The spectrum of HIV related ocular manifestation varies by geographic location and with opportunistic infection related eye diseases more common in South Asia compared to Sub Saharan Africa.^{13,14}

REVIEW OF LITERATURE

IMMUNOLOGY:

There are two types of HIV i.e. Type1 and Type2. Type1 is more common. The subtypes of HIV-1 which are more prevalent in India are A, B and C. The virus is 120 nm in diameter and consists of an outer envelope of glycoprotein, a core shell and a cone shaped inner core containing reverse transcriptase enzyme.¹⁵

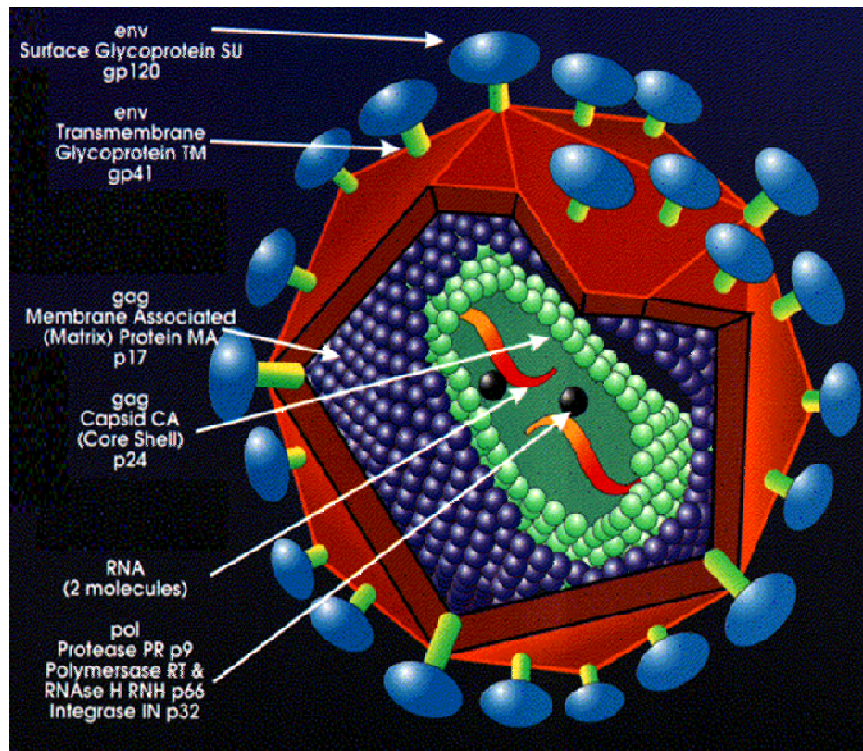
Lymphocytes in blood are divided into T (thymus derived) and B (bone marrow derived) the former forming 65-80% and the latter forming 5 to 15% of peripheral blood lymphocyte. T cells are classified into CD4+ helper T cells and CD8+ cytotoxic T cells, the former are predominantly affected in HIV infected patients. CD4+ T cells are divided into two types according to their cytokine production.¹⁶ HIV can destroy the CD4+ T cells by binding to both the CD4+ receptor and a co receptor (two types of co-receptors i.e. CCR-5 for macrophage tropic and fusin for T cell tropic) and integrating itself into the host DNA after conversion of viral RNA into double stranded DNA. Normal CD4+ counts are between 300 to 1000 cells/cu.mm. Functional defects in B lymphocytes occur in the early course of infection due to which

deficient antibody response to new antigens occur despite hypergammaglobulinemia.¹⁷

Correlation of CD4 cell count and HIV associated ocular disease.^{17,18,19}

CD4 count (cells/cu.mm)	Disease
<500 up to 250	<ul style="list-style-type: none"> • Kaposi sarcoma • Ocular tuberculosis
<250	<ul style="list-style-type: none"> • Pneumocystosis • Toxoplasmosis • Retinal/conjunctival micro vasculopathy
<100	<ul style="list-style-type: none"> • Keratoconjunctivitis sicca
<50	<ul style="list-style-type: none"> • Intra ocular lymphoma • HIV associated uveitis • Cryptococcal choroiditis • Cidofovir & Rifabutin induced uveitis • Necrotizing herpetic retinitis (CMV, VZV)
At any CD4 count	<ul style="list-style-type: none"> • Herpes zoster keratouveitis • Molluscum contagiosum • Endogenous endophthalmitis

Structure of HIV



OCULAR MANIFESTATIONS OF HIV INFECTION - ETIOLOGY

The ocular manifestations in HIV infected patients may result from the following.¹⁷

1. The underlying infection itself – ex. HIV induced retinopathy
2. Opportunistic infections –ex. CMV retinitis.
3. Neoplasms due to impaired surveillance – ex. Intra ocular lymphoma.
4. Complications arising from treatment – ex. Cidofovir induced uveitis.

5. Altered immune regulation giving rise to autoimmune phenomenon – ex. Keratoconjunctivitis sicca.

OPHTHALMIC DISORDERS ASSOCIATED WITH HIV INFECTION.^{20,21}

I. Non-infectious vasculopathy

A. Microvasculopathy

- i. Retina -“HIV retinopathy”
- ii. Conjunctival microvasculopathy
- iii. Optic nerve

B. Macrovasculopathy

- i. Retina
 - a) Venous occlusions
 - b) Arterial occlusions

II. Infections

A. Ocular surface and adnexa

- i. Molluscum contagiosum virus dermatitis, blepharitis
- ii. Herpes zoster ophthalmicus
- iii. Herpes simplex virus keratitis
- iv. Microsporidial Keratoconjunctivitis
- v. Bacterial and fungal keratitis

B. Retina and choroid

- i. Cytomegalovirus retinitis

- ii. Varicella zoster virus retinitis
- iii. Herpes simplex virus retinitis
- iv. Syphilitic uveitis/retinitis
- v. Toxoplasma Gondi retinochoroiditis
- vi. Pneumocystis carinii choroidopathy
- vii. Mycobacterium tuberculosis choroiditis
- viii. Histoplasmosis

C. Orbital infections

- i. Preseptal cellulitis

III. Neoplasms

A. Eyelid/ocular surface

- i. Kaposi's sarcoma
- ii. Lymphoma
- iii. Squamous cell carcinoma

B. Intraocular

- i. Lymphoma

C. Orbit

- i. Lymphoma
- ii. Kaposi's sarcoma (rare)

IV. Neuro-ophthalmologic abnormalities associated with intracranial or orbital diseases

A. Infections

- i. Cryptococcal meningitis
- ii. Intracranial toxoplasmosis
- iii. Progressive multifocal leukoencephalopathy
- iv. Varicella-zoster virus infection
- v. Syphilitic meningitis
- vi. Tuberculosis meningitis

B. Neoplasms

- i. Intracranial lymphoma

V. Adverse effects of systemic drugs

A. Uveitis

- i. Cidofovir
- ii. Fomivirsen
- iii. Rifabutin

B. Optic neuropathy

- i. Ethambutol

C. Retinopathy

- i. Didanosine

VI. Auto immune phenomenon:

A. Kerato conjunctivitis sicca

ANTERIOR SEGEMENT AND ADNEXAL MANIFESTATIONS

A. HERPES ZOSTER OPHTHALMICUS:

It is caused by varicella zoster virus (VZV) which on primary infection causes chickenpox and on reactivation causes zoster. Herpes zoster usually occurs in 10 to 20% of the infected individuals with VZV. The virus remains latent in the sensory neurons, of which mostly is detected in the trigeminal nerve. Upon its reactivation in the ophthalmic division of the trigeminal nerve herpes zoster ophthalmicus (HZO) occurs. In a study conducted by Hodge and associates, they found the individual risk of obtaining HZO in HIV infected persons is 6.6:1 compared to non-infected persons.^{13,7}

A study by *Sellitti et al* showed that HZO in HIV infected persons is of severe, long duration, more complications, increase in hospitalization and increases in rate of recurrence compared to non HIV infected persons.^{13,22} There has also been an increase in incidence of HZO in patients who are on HAART immediately after treatment with protease inhibitors, which was proved by *Martinez and his associates*.^{13,23} This was due to the immune recovery phenomenon. A case of herpes zoster ophthalmicus with orbital apex syndrome has been reported as an initial manifestation of HIV infection in a case report.²⁴

B. VIRAL KERATITIS:

The most common causes of infectious keratitis in HIV infected persons are VZV and herpes simplex virus (HSV).²⁵ The incidence of VZV keratitis in individuals with HZO was found to be 65% and for dendritiform lesions it is about 51%.^{13, 26} Compared to non HIV infected persons, HIV infected persons are more likely to experience corneal involvement and at increased chances for perforation.^{13,25} In a study by *Engstrom and Holland*, they found that HIV infected persons will experience chronic keratitis due to VZV. Lesions in chronic VZV keratitis often become more pleomorphic with thickened opaque epithelium.^{13,27} Corneal stromal involvement has been seen rarely in HIV infected persons and this can be attributable to T cell dysfunction which may be protective against stromal keratitis.¹³ In a study done by *Young and associates*, they found the atypical presentation of epithelial keratitis in HIV infected persons which include marginal location, mean healing time of 3 weeks, relative resistance to treatment, lengthier recurrences.^{13,27} Patients with HZO on HAART may develop VZV stromal keratitis and it occurs due to immune recovery. In a case report by *Naseri and Margolis*, a patient with resolved HZO developed stromal keratitis on HAART as T cells presumably

recognized and responded to VZV antigens in the corneal stroma and cause stromal keratitis.^{13,28}

CMV (cytomegalo virus) can cause both epithelial and stromal keratitis, but both being very rarely seen even though CMV is the most common opportunistic infectious agent among HIV infected patients.^{13,29} The incidence of corneal endothelial deposits among found patients with CMV retinitis is about 80%.^{13,30} These are mostly seen in the inferior cornea in linear, stellate, reticulate pattern and are composed of fibrin and macrophages.¹³

C. BACTERIAL KERATITIS:

Despite the presence of normal ocular flora, the risk of infections with normal flora itself is great in HIV infected patients.¹³ *Pseudomonas aeruginosa*, *Staphylococcus aureus* and *Staphylococcus epidermidis* are more commonly found in HIV infected persons.^{13,31} The factors responsible for these infections for presence of concomitant dry eye and healed viral keratitis which causes epithelial defect and pave way for the normal flora.¹³ Their clinical significance being they are more bilateral, multi pathogenic and more prone for perforation.^{13,32} Low level of inflammation plays a role in delay in treatment.¹³ In case of

coinfection with *Neisseria gonorrhea*, HIV can modify the host response resulting in more severe clinical features.^{13,33}

D. FUNGAL KERATITIS:

In contrast to normal population where history of trauma plays as a predisposing factor to fungal corneal ulcer, it develops spontaneously in HIV infected persons. *Candida* and *Cryptococcus* are the common causes. *Cryptococcus* commonly causes meningitis and choroiditis but cases of iris granuloma, scleral perforation have also been noted.^{13,34} In HIV infected persons they run a more protracted course, often bilateral and can lead to corneal perforation.³⁵ Polymicrobial keratitis has been reported as an initial manifestation of HIV infection. In a case report by *Radhika et al*, in which they reported a case of spontaneous ulcerative keratitis caused by coagulase negative *Staphylococcus*, *Fusarium* and *Acanthamoeba* in a same patient.³⁶

E. MICROSPORIDIAL KERATITIS:

Microsporidia are spore forming, obligate, intracellular parasites. Microsporidial keratitis should be suspected in HIV infected persons in whom repeated culture for epithelial keratitis comes as negative.¹³ It is typically characterized by bilateral superficial punctate keratitis, intra epithelial white infiltrates, mild anterior chamber reaction

and follicular hypertrophy.^{13,37} They typically cause systemic manifestations when the CD4 count fall below 100 cells per cu.mm.¹³

F. MOLLUSCUM CONTAGIOSUM:

It is seen in 5% of HIV infected patients, caused by a pox virus and has an incubation period of 6 to 8 weeks.¹³ It is characterized by pink or pearly white nodules on the skin. The major clinical significance in HIV infected persons is that Mollusca occurs as larger in number and size over lids and conjunctiva, confluent, more resistant to therapy with more chances of recurrence. A **chin-strap distribution** is more common in HIV infected patients.¹³ It has been reported as the initial manifestation of HIV infection.¹³

G. TOXOPLASMIC UVEITIS:

In HIV infected persons a primary anterior uveitis can occur even without the presence of retinal lesions, though in immune competent persons it can occur only as a secondary phenomenon.^{13,38} Severe anterior segment inflammation with iris nodules and destruction has been noted¹³

H. ANTERIOR UVEITIS:

Anterior uveitis as an isolated symptomatic disorder is very rare in HIV infected persons. In a study conducted by *Verma et al*, it was concluded that anterior uveitis not very symptomatic in HIV infected patients. They followed a group of 172 HIV positive patients, among whom only 12 patients had symptomatic anterior uveitis.³⁹ Mild iridocyclitis in HIV infected persons is commonly due to posterior segment disease most common being CMV retinitis as demonstrated by *Cunningham and Margolis*.⁴⁰

I. SYPHILITIC UVEITIS:

It is the most common cause of bacterial uveitis in HIV infected patients and its prevalence was found to be about 0.6%. The clinical significance in HIV infected persons is that it causes pan uveitis with more severe anterior segment inflammation.¹³ As compared to immune competent hosts, ocular syphilis in HIV positive persons has a more protracted course and severe clinical features.¹³ Other manifestations being chancres of conjunctiva, gumma and conjunctivitis with the latter being histologically similar to sarcoidosis.¹³

MYCOBACTERIUM RELATED ANTERIOR SEGMENT DISORDERS:

There is no change in type of anterior segment lesions caused by TB in HIV infected and non-infected people. Common presentations include granular masses, polypoid tumours, ulcers, granulomatous uveitis and chronic red eye.^{13,41} It can also present as interstitial keratitis, nodular scleritis, and sclerokeratitis.

J. ADNEXAL INFECTIONS:

Preseptal cellulitis due to staphylococci has been found in HIV infected persons due to the presence of twice the number of staphylococci in nasal mucosa compared to normal individuals.¹³ Lid abscesses due to staphylococci, CMV in association with Molluscum contagiosum has also been found in HIV infected persons. Blepharitis is more common and has been reported as an initial manifestation of HIV infection along with lid ulcer in a case report.⁴²

K. CONJUNCTIVAL MICROVASCULOPATHY:

Almost 3/4th of HIV infected persons have some form of conjunctival microvasculopathy which include:

1. Segmental narrowing and dilatation

2. Visible granularity in the blood column
3. Comma shaped granular fragment
4. Micro aneurysm formation.¹³

These changes have more correlation with the occurrence of HIV retinopathy and more commonly occur in the inferior limbus area. The exact etiology is still unknown and it may be due to immune complex deposition, increased viscosity of the blood or due to direct effects of the virus itself.¹³

L. KERATOCONJUNCTIVITIS SICCA:

It occurs in the later stage of the disease and in about 20 to 30% of affected individuals. The etiology is due to inflammatory destruction of the main and accessory lacrimal glands due to lymphocytic infiltration and direct damage of the conjunctival surface by the virus itself.¹³

It predisposes to secondary bacterial keratitis due to epithelial defects and spontaneous corneal thinning with perforation can also occur due to the virus itself.¹³

A case of keratomalacia with Xerophthalmia has been reported as an initial manifestation of HIV infection in a case report by *Cynthia et al.*⁴³ Vitamin A deficiency even though rare in adults can manifest commonly in HIV infected individuals.

M.NEOPLASMS OF THE ADNEXA:

In the western world Kaposi's sarcoma is the most common adnexal neoplasm associated with HIV, whereas in India it is uncommon due to the low prevalence of human T cell lymphotropic virus (HHV 8). In the African countries it's the squamous cell carcinoma of conjunctiva which is more common. Kaposi's sarcoma has been included as one of the presentation in diagnosing AIDS defining illness.

1. KAPOSI'S SARCOMA:

Kaposi's sarcoma is a vascular mesenchymal tumor appearing as red velvet nodules on the ocular surface. It occurs mostly in the inferior fornix and histologically shows incomplete vascular spaces without endothelium surrounded by malignant spindle cells which are of endothelial origin.⁴⁴ The classification of adnexal Kaposi's sarcoma has been given by *Dugel and his colleagues* who divided it into three types.

Type 1 and 2 lesions are patchy, flat, less than four months of duration and less than 3 mm in height, whereas type 3 lesions are more than four months duration and more than 3 mm in height. Conjunctival Kaposi's sarcoma may mimic sub conjunctival hemorrhage or as an elevated purple red mass, whereas Kaposi's sarcoma on eyelids may mimic like other lesions elsewhere in the body.

2. SQUAMOUS CELL CARCINOMA:

Most common presentations of squamous cell carcinoma include¹³

- Nasal location
- Faster growth
- Size greater than 1 cm
- Changes in color
- Corneal over riding.

In a study done by *Chisi et al* the estimated prevalence of squamous cell carcinoma in HIV positive patients is 7.8%. He evaluated 409 HIV positive patients between 25 to 53 years and detected 103 patients with conjunctival growths, of whom 32 had histologically proven squamous cell carcinoma.⁴⁵ HIV testing, should be carried out in all patients with squamous cell carcinoma who live in high risk areas as it may be the first sign of HIV positivity.

3. NON HODGKIN'S LYMPHOMA:

Non-Hodgkin's lymphoma tends to be of higher grade and occur in 5% of HIV positive patients. NHL can mimic as kerato conjunctivitis sicca and anterior chamber reactions can occur with intra ocular lymphoma. Primary NHL can present as proptosis, ptosis, gaze paresis, internal ophthalmoplegia.⁴⁶

N. IMMUNE RECOVERY UVEITIS:

Immune recovery uveitis is a phenomenon noted as a part of *immune reconstitution syndrome (IRIS)* occurring in patients on HAART. Before the introduction of HAART people with CMV retinitis had CD4 count less than 50/cu.mm and minimal intra ocular inflammation. Immune recovery uveitis mainly involves the anterior uvea and vitreous and is associated with marked disturbance of visual function and more inflammation. It occurs as a phenomenon to old CMV antigens on their path to immune recovery, hence it is more important to recognize this condition among people on HAART.⁴⁷

O. DRUG INDUCED UVEITIS:

A predominantly anterior uveitis occurs as a toxic effect of Rifabutin and Cidofovir with discrepancy between morphological changes and clinical symptoms.⁴⁸ Rifabutin is used as a prophylactic agent and as an anti-mycobacterial agent, while Cidofovir is used for CMV and other group of herpes viruses. The incidence of Rifabutin induce uveitis is less than 0.01% when used at a dosage of 300 mg/day and its incidence is increased when used at the rate of more than 450 mg/day.⁴⁹ The incidence of Cidofovir induced uveitis is high when the intravitreal dose is greater than 40 µg, whereas the incidence is low when the intravitreal

dose is less than 20 µg. The incidence of Cidofovir induced uveitis is more when it is used concomitantly with protease inhibitors due to potential drug interactions.⁵⁰

POSTERIOR SEGMENT MANIFESTATIONS:

Posterior segment manifestations are more common in HIV infected persons than other manifestations.⁵¹ The spectrum of manifestations varies demographically with opportunistic infections related manifestations common in developed countries than in developing countries.

A. HIV RETINOPATHY(MICRO VASCULOPATHY):

It is the most common ocular manifestation seen in about 60% of HIV infected persons.⁵² It is characterized by the presence of cotton wool spots which are located more around the posterior pole.

They represent infarct in the nerve fiber layer and consist of yellowish patches with more rounded borders found along the vascular arcade in the posterior pole with no associated hemorrhages or areas of necrosis. Most patients are asymptomatic and severity varies according to the location of lesion. The occurrence of HIV retinopathy is inversely related to the CD4 Count.

B. MACRO VASULOPATHY:⁵¹

Large vessel occlusions though very rare can occur in association with necrotizing retinitis, infiltrative lymphomatous optic neuropathy and as an isolated disorder. A case of central retinal vein occlusion due to herpetic necrotizing retinitis has been reported as the initial manifestation of HIV infection in a case report.⁵³

C. OPPORTUNISTIC INFECTIONS:⁵¹

Opportunistic infections of the posterior segment can occur as a unifocal or multifocal choroiditis but more commonly as a necrotizing retinitis.

Retinitis in inflamed eyes usually occur with higher CD4 counts and are commonly due to acute retinal necrosis(ARN), syphilis, Cryptococcus and toxoplasmosis, whereas retinitis in quiet eyes is commonly due to CMV and progressive retinal necrosis. (PRN)

1) CYTOMEGALO VIRUS RETINITIS:²⁰

CMV retinitis is by far the most common opportunistic intraocular infection in people with AIDS. In a study done by *Lim et al*, who reviewed the spectrum of ophthalmic manifestations of 118 HIV positive individuals in Singapore between May 1995 to October 1996 and found

that CMV retinitis was the most common cause of visual loss found in 37 patients.⁵⁴ CMV retinitis is rarely the first manifestation of AIDS as it occurs mostly in patients who have CD4+ T-lymphocyte counts of less than 50 cells/cu.mm at diagnosis. One study found that 85% of people with extra ocular CMV infection developed CMV retinitis after a mean follow-up period of 6.4 months. Heterosexual men are less likely than homosexual men to develop CMV retinitis, perhaps because homosexuals have a higher rate of pre-existing CMV infection. CMV retinitis remains a major cause of morbidity in HIV-infected people. CMV retinitis may begin with infection of retinal vascular endothelial cells, with subsequent spread to adjacent glial and neuronal cells as well as to RPE, although early autopsy studies failed to identify infected endothelium in all cases. The diagnosis of CMV retinitis is based on clinical signs and symptoms with most patients being asymptomatic if it is unilateral. One study found that over half of new cases of CMV retinitis were diagnosed during routine screening eye clinic visits and that over 75% of affected patients were asymptomatic at the time of diagnosis. Hence routine screening has been recommended every 3 months in patients with CD4 count less than 50/cu.mm.⁵⁵

There are three clinical forms – classical, indolent, frosted branch angitis.⁵⁶ The classical form is characterized by areas of confluent

necrosis with hemorrhage that develops along the vascular arcade giving rise to a “*pizza pie*” or “*cottage cheese*” appearance. The advancing edges of the lesions spread contiguously and very sharp which untreated gives rise to full thickness gliosis and atrophy. The indolent form is noted as a granular lesion in the peripheral retina and has less dense opacification without any hemorrhage. Bilateral involvement occurs in 30% to 40% of cases at diagnosis. There are usually mild anterior chamber and vitreous inflammatory reactions, and fine keratic precipitates are often seen.

The natural history of CMV retinitis is progressive with eventual destruction of the entire retina occurs within 6 months. Untreated lesions enlarge slowly; spread toward the fovea occurs at a median rate of only 24 $\mu\text{m}/\text{day}$ or approximately 750 μm every three weeks and is somewhat faster toward the ora serrata.⁵⁷ Rhegmatogenous retinal detachment is more common with CMV retinitis, occurring in 13 to 29% of patients and can occur either in active or healed phase of the disease. The risk of occurrence of retinal detachment and immune recovery uveitis is directly proportional to the area of involvement of CMV retinitis.

2) NECROTISING HERPETIC RETINITIS:

It is a spectrum of retinitis induced by herpes viruses most commonly by VZV. It includes two types –

1. Acute retinal necrosis (ARN)
2. Progressive retinal necrosis (PRN).

1. ACUTE RETINAL NECROSIS:⁵⁷

It is a devastating necrotizing retinitis which affects males more than females in the ratio 2:1 and is biphasic disease, tends to be caused by HSV in younger individuals and by VZV in older individuals. Presentation is usually unilateral with vitritis and granulomatous anterior uveitis being found in almost all cases. Retinitis includes peripheral retinal periarteritis associated with multifocal deep yellow white retinal infiltrates. Gradual coalescence of infiltrates with full thickness necrosis and circumferential progression occurs. The posterior pole is usually spared till late. Acute lesions resolve within 6 to 12 weeks leaving transparent necrotic retina with hyper pigmented borders. The second eye is involved in 30% usually within 2 months unless treated. Prognosis is relatively poor particularly with VZV with 60% of patients having a

final visual acuity less than 6/60 due to retinal detachment, ischemic optic neuropathy and occlusive periphlebits.⁹⁵

2. PROGRESSIVE RETINAL NECROSIS:⁵⁷

It is caused by VZV and behaves aggressively as a consequence of profound immune suppression. Presentation is with rapidly progressive visual loss which is usually unilateral and characterized by minimal anterior uveitis and vitritis, yellow white retinal infiltrates, rapid confluence and full thickness retinal necrosis with early involvement of macula. Vitreous inflammation is usually late and reflects extensive retinal necrosis.

D. TOXOPLASMOSIS:

In HIV infected persons, toxoplasmosis occurs as a primary infection rather than reactivation. In contrast to immune competent persons, it is usually multi focal, bilateral and rarely associated with chorioretinal scars. It may cause other abnormalities like vitritis, iritis, papillitis, retro bulbar neuritis and outer retinal toxoplasmosis.⁵⁸ In contrast to CMV retinitis it is associated with more severe intra ocular inflammation and less hemorrhages.

E. CHOROIDITIS:

1) TUBERCULOSIS:⁵¹

Choroiditis associated with tuberculosis can present either as multifocal choroidal tubercles with discrete yellow lesions at the posterior pole or it can present as a solitary posterior pole granuloma like mass lesion. Though pulmonary tuberculosis is commonest systemic opportunistic infection in India, the incidence of ocular tuberculosis among HIV infected persons is very low. In a study conducted by *Alay banker et al*, in 1286 cases of HIV infected persons the incidence of ocular tuberculosis is found to be 1%.⁵⁸

2) CRYPTOCOCCAL CHOROIDITIS:

It can be solitary or confluent, multifocal and may be associated with granulomatous iritis, iris mass, necrotizing retinitis, endophthalmitis, conjunctival mass, eyelid nodule and optic neuritis.⁵¹ Meningitis associated with *Cryptococcus* is the most common cause of Neuro ophthalmic manifestation of HIV associated ocular disease.

3) PNEUMOCYSTIS CHOROIDITIS:⁵⁷

Pneumocystis jiroveci is the major cause of mortality and morbidity in AIDS. The presence of choroidal involvement can be an important feature of extra pulmonary systemic dissemination.

Presentation includes flat, yellow, round choroidal lesions scattered throughout the posterior pole which are frequently bilateral and not associated with vitritis. The lesions may coalesce and produce large geographic patches. Even when the fovea is involved the visual impairment is little.

4) MALIGNANCY INDUCED CHOROIDITIS:

Non-Hodgkin's lymphoma can produce necrotizing retinitis, multifocal choroiditis, retinal vasculitis, vitritis, sub retinal mass and pseudo hypopyon uveitis.⁵⁹

5) SYPHILIS:

Ocular syphilis may present as iritis, vitritis, retro bulbar optic neuritis, papillitis, retinal vasculitis, necrotizing retinitis which may be clinically indistinguishable from CMV and exudative retinal detachment.⁶⁰

NEURO OPHTHALMOLOGICAL MANIFESTATIONS:⁶¹

The incidence of nervous system involvement is about 50% in HIV infected persons resulting in different patterns of neurological involvement at some point during the course of the disease. The incidence of Neuro ophthalmological disorders is about 3 to 8%.⁶² The

various Neuro ophthalmological manifestations include optic neuropathy which may be Neuro retinitis, anterior optic neuropathy or retro bulbar neuritis, abnormal movement of saccades or pursuits, ocular motor palsy, gaze palsy, visual field defects, papilledema, optic atrophy, cortical blindness. The causes include cerebral toxoplasmosis, Cryptococcal meningitis, tuberculous meningitis, AIDS related dementia complex, cerebral lymphoma and herpes zoster encephalitis. Sometimes these may be the presenting feature of otherwise asymptomatic HIV infected person. A case of isolated homonymous hemianopia due to presumptive cerebral tuberculosis has been manifested as an initial presentation of HIV infection in a case report by *Sujit gharai et al.*⁶³

I. OCULAR MOVEMENT DISORDER:

In a study done by *Sweeney et al*, they found that seropositive patients demonstrated disturbances in pursuit movements that were correlated with the extent of immunosuppression. They noted that oculomotor disturbances are present in HIV positive individuals even before they develop manifestations of marked AIDS dementia complex. Due to this, they suggested quantitative eye movement studies may provide a useful Neuro behavioral procedure for characterizing and monitoring the progression of CNS involvement associated with HIV

infection from early in its course. In asymptomatic patients they represent the early manifestation of HIV infection.⁶⁴

II. OPTIC NEUROPATHIES:

Optic neuropathies in HIV infected persons can occur due to infectious, compressive and inflammatory etiologies. Recent evidence support HIV by itself can produce optic neuropathy. Optic nerves of HIV infected persons can undergo chronic degeneration resulting in axonal loss. In a study by Sadun et al, they found that axonal degeneration was noted in association with mononuclear cell infiltration in sections of optic nerve of HIV positive individuals suggesting the role of HIV itself in the pathogenesis of primary optic neuropathy.⁶⁵ Current theories emphasize the importance of tumor necrosis factor alpha in the evolution of primary HIV optic neuropathy.

III. CRANIAL NERVE PALSY:

In a study conducted by *Mwanza et al*, the prevalence of cranial nerve palsy is 25%. The most common nerves to be involved are sixth and third. Even though toxoplasmosis and cryptococcosis are the most common causes, the exact cause is complicated by the presence of multiple underlying etiologies.⁶⁶

IV. ABNORMALITIES IN VISUAL EVOKED POTENTIAL:

The incidence of subclinical abnormal VEPs (Visual evoked potential) has been reported to be around 3 to 49% in HIV infected persons. Though completely normal VEPs have been found in both neurologically symptomatic and asymptomatic individuals.⁶⁷ There is evidence that, despite normal visual acuity HIV infected persons may have subclinical dysfunction of the visual pathways which can be detected using electro physiological methods.⁶⁸

OBJECTIVES OF THE STUDY:

1. To determine the ocular manifestations of HIV infection occurring in adults at the time of diagnosis.
2. To estimate the prevalence of ocular manifestations occurring at the time of diagnosis.
3. To determine visual impairment associated with HIV related ocular manifestations.
4. To correlate the ocular manifestations with the demographic profile and clinical stage of the disease at the time of diagnosis.

MATERIALS AND METHODS:

STUDY DESIGN:

It is a hospital based cross sectional study.

STUDY PERIOD:

The study was done between the periods from September 1, 2011 to September 1, 2012.

STUDY POPULATION:

The study was done among people who attended the Outpatient clinic of Department of sexually transmitted diseases (STD) and ART Centre, who are newly diagnosed as seropositive for HIV.

STUDY METHODS:

Before commencing the study, Ethics committee approval was obtained from the Ethics committee of Coimbatore medical college and government hospital. Patients were screened at outpatient clinic twice in a week for newly detected seropositivity for HIV. After they underwent counseling, they were explained about the ocular manifestations which may occur during the course of the disease and the need for ophthalmic screening. After obtaining clear consent (oral

consent was used in the present study) the patients were enrolled for the study. For maintaining the confidentiality of the patient, names of the patient were neither disclosed any other person nor published in any written form. Even the registration number in the ART clinic which is unique to each patient was neither disclosed nor published. Instead the outpatient number of OP clinic of ophthalmology was used as the reference number. The inclusion and exclusion criteria used were as follows:

INCLUSION CRITERIA:

1. Age > 19 Years and < 65 years,
2. Newly diagnosed patients of HIV seropositivity, with blood investigation confirmed at VCTC, CMCH.
3. Patients diagnosed as HIV positive outside centres who came to attend ART centre are also included
4. Patients who are referred from other department to VCTC centre for screening purposes.

EXCLUSION CRITERIA:

1. Children and < 19 years.
2. Pregnant women
3. Persons who are terminally ill.

4. Persons who are unable to give consent due to Neuro behavioral problems.
5. Persons who are not willing for giving consent because of confidentiality loss.

After making sure the patient falls under the above criteria, patients were brought to the OP clinic of Ophthalmology department and registered. They were undertaken for the following protocol

1. A thorough history taking was taken – first regarding the demographic profile of the patient including
 - Age
 - Occupation
 - Income
 - Marital status
 - Sexual history
 - Associated history of tuberculosis
 - Drug abuse/blood transfusion
2. Patients were asked about the presence or absence of ocular symptoms.
3. The socio economic status of the patient was found by using modified Kuppuswamy grading scale.

4. Presence or absence of systemic symptoms was asked and clinical stage of HIV was determined using WHO grading of clinical stage of HIV disease.
5. CD4 count value which was determined at the time of diagnosis was noted.
6. The patient was then subjected to a routine ophthalmic examination which includes the following:
 - Best corrected visual acuity was determined using Snellen's chart.
 - Any evidence of previous refractive error was also noted.
 - A central field charting was done using Bjerrum screen
 - A simple torch light examination was performed to look at the lids and adnexa.
 - A slit lamp examination was done to determine the anterior segment.
 - A Schirmer's test to determine the tear film status was done
 - After dilatation with 1% Tropicamide a detailed fundus examination was done using direct ophthalmoscope, 90D lens attached with slit lamp and an indirect ophthalmoscope.

7. All findings were noted and the final ophthalmic status was noted.
8. In case of getting abnormal findings, it was examined and confirmed by another person. In this study it was done by the guide of the study.
9. To avoid bias, above things were done only by the principal investigator alone.
10. The ophthalmic status was revealed to the patient after necessary counseling and need for periodic review was suggested.
11. Since the study was a cross sectional study (single time study) reviews of the patients were not conducted exclusively by the investigator to avoid bias. The enrollment of the patient under the study was not revealed to others.
12. At the end of the study period the data were given to an investigator for statistical analysis.

WHO CLINICAL STAGING OF HIV/AIDS FOR ADULTS AND ADOLESCENTS WITH CONFIRMED HIV INFECTION⁶⁹

Clinical stage 1

- Persistent generalized lymphadenopathy
- Asymptomatic

Clinical stage 2

- Recurrent respiratory tract infections
- Moderate unexplained weight loss <10% of presumed or measured body weight
- Herpes zoster
- Recurrent oral ulceration
- Angular cheilitis
- Papular pruritic eruptions
- Seborrhoeic dermatitis
- Fungal nail infections

Clinical stage 3

- Unexplained persistent fever (above 37.6°C intermittent or constant, for longer than one month)
- Unexplained chronic diarrhea for longer than one month

- Unexplained severe weight loss (>10% of presumed or measured body weight)
- Persistent oral candidiasis
- Oral hairy leukoplakia
- Pulmonary tuberculosis (current)
- Severe bacterial infections (such as pneumonia, empyema, pyomyositis, Bone or joint infection, meningitis or bacteremia)
- Acute necrotizing ulcerative stomatitis, gingivitis or periodontitis
- Unexplained anemia, neutropenia Or chronic thrombocytopenia .

Clinical stage 4

- HIV wasting syndrome
- Pneumocystis pneumonia
- Recurrent severe bacterial pneumonia
- Chronic herpes simplex infection (orolabial, genital of more than one month's duration or visceral at any site)
- Esophageal candidiasis (or candidiasis of trachea, bronchi or lungs)
- Extra pulmonary tuberculosis
- Kaposi's sarcoma
- Cytomegalovirus infection (retinitis or infection of other organs)
- Central nervous system toxoplasmosis

- HIV encephalopathy
- Extra pulmonary Cryptococcosis including meningitis
- Disseminated non-tuberculous mycobacterial infection
- Progressive multifocal leukoencephalopathy
- Chronic cryptosporidiosis (with diarrhea)
- Chronic Isosporiasis
- Disseminated mycosis (Coccidiomycosis or Histoplasmosis)
- Recurrent non-typhoidal Salmonella bacteremia
- Lymphoma (cerebral or B-cell non-Hodgkin) or other solid HIV-associated tumors.
- Atypical disseminated leishmaniasis
- Symptomatic HIV-associated nephropathy or symptomatic HIV-associated cardiomyopathy.
- Invasive cervical carcinoma

MODIFIED KUPPUSWAMY GRADING OF SOCIO ECONOMIC STATUS:

It consists of three variables

1. Profession
2. Per capita income
3. Occupation

Each variable is given a score depending on the data. Finally all three are added to give a cumulative variable, which is categorized according to the score.

Education	Score
Professional	7
Graduate	6
Intermediate	5
High school	4
Middle school	3
Primary	2
Illiterate	1

Occupation	Score
Professional	10
Semiprofessional	7
Clerical, shop owner, farmer	5
skilled	4
Semi-skilled	3
unskilled	2
unemployed	1

Family income per month	Score
>17520	12
8760-17515	10
6570-8750	6
4380-6560	4
2628-4370	3
885-262	2
<87	1

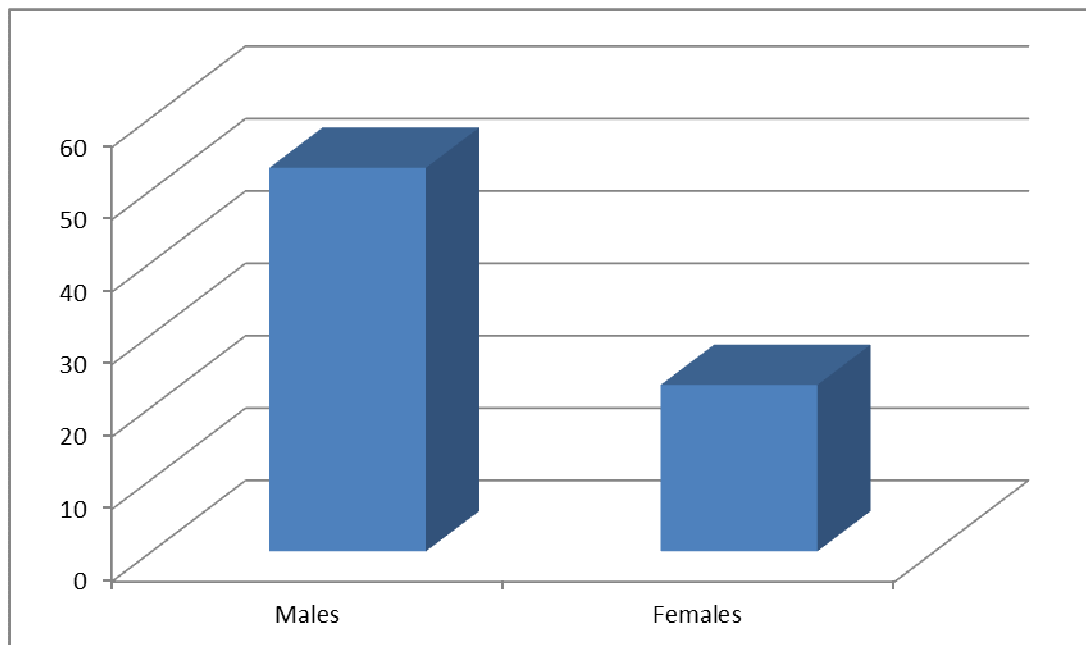
Total score	Socio economic status
26 to 29	Upper I
16 to 25	Upper middle II
11 to 15	Lower middle III
5 to 10	Upper lower I V
< 5	Lower V

STATISTICAL ANALYSIS:

- NUMBER OF PERSONS ENROLLED FOR THE STUDY: 76
- NUMBER OF EYES EXAMINED : 152

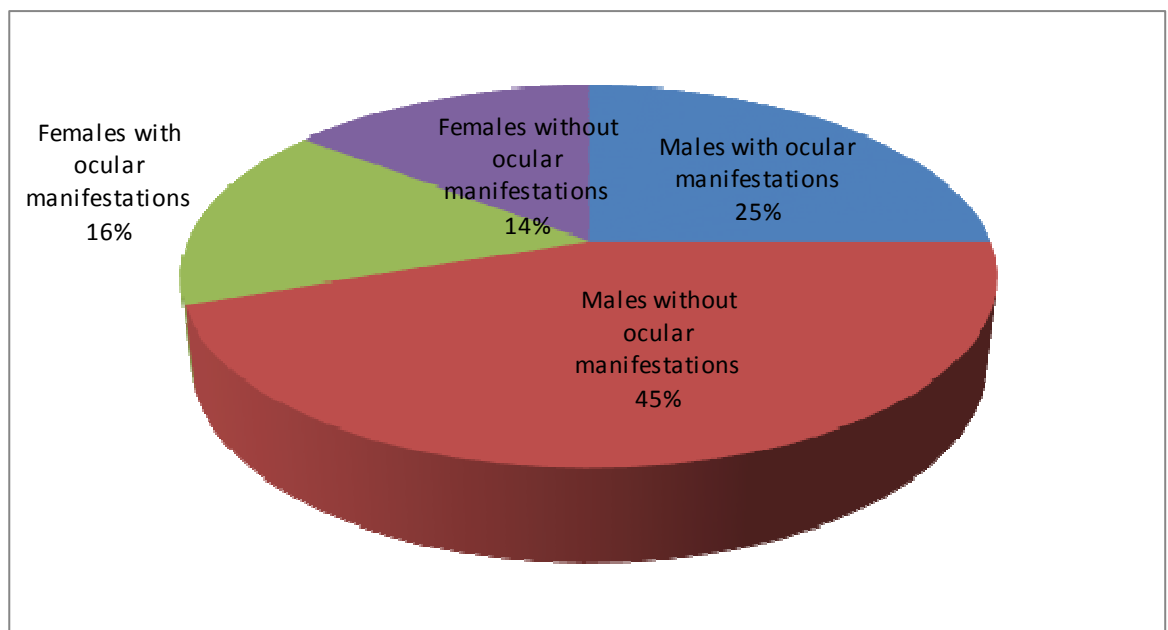
GENDER:

- NUMBER OF MALES: 53
- NUMBER OF FEMALES: 23



GENDER	Without ocular manifestations	With ocular manifestations	Total
Males	34	19	53(69.7%)
Females	12	11	23(30.3%)
	46(60.5%)	30(39.5%)	76

The Chi-square value of the above chart is 0.963 and the 'P' value is 0.326



SOCIO ECONOMIC STATUS:

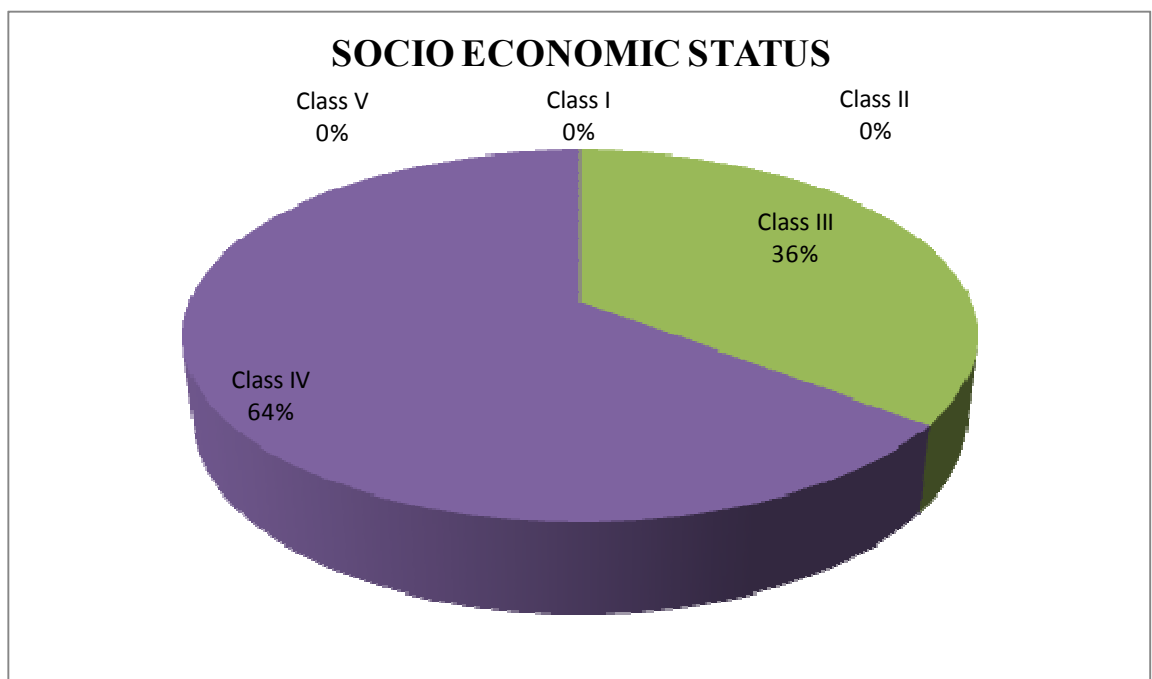
CLASS 1: 0

CLASS 2: 0

CLASS 3: 27

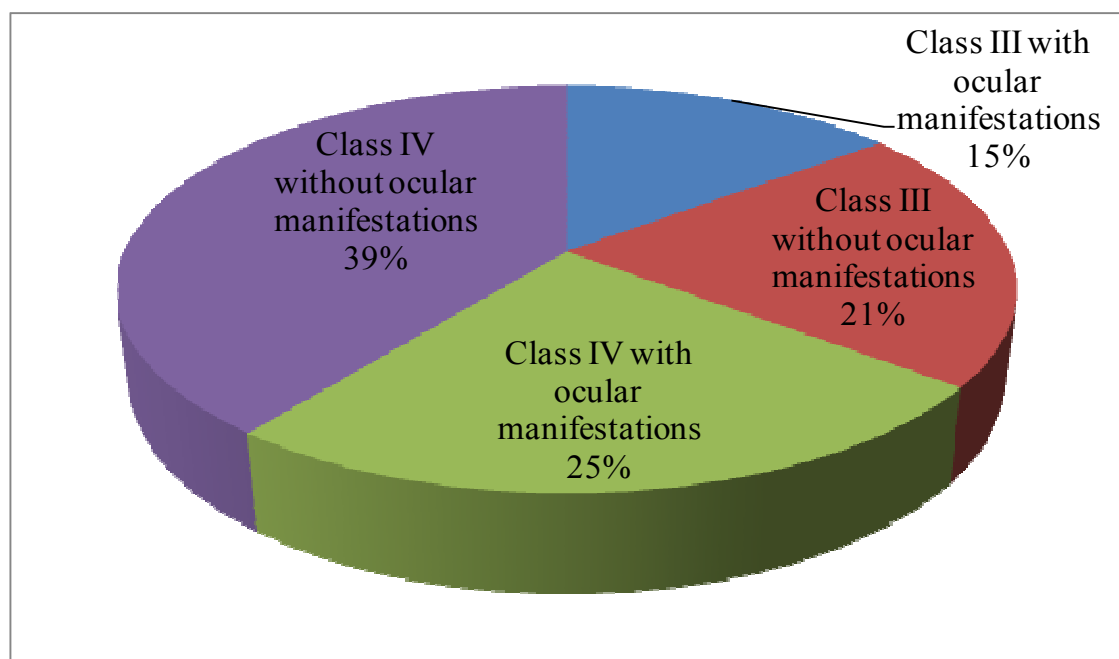
CLASS 4: 49

CLASS 5: 0



Socio economic status	Without ocular manifestations	With ocular manifestations	Total
III	16	11	27
IV	30	19	49
Total	46	30	76

The Chi-square value for the above chart is 0.028 and the “P” value is 0.867



AGE GROUPS:

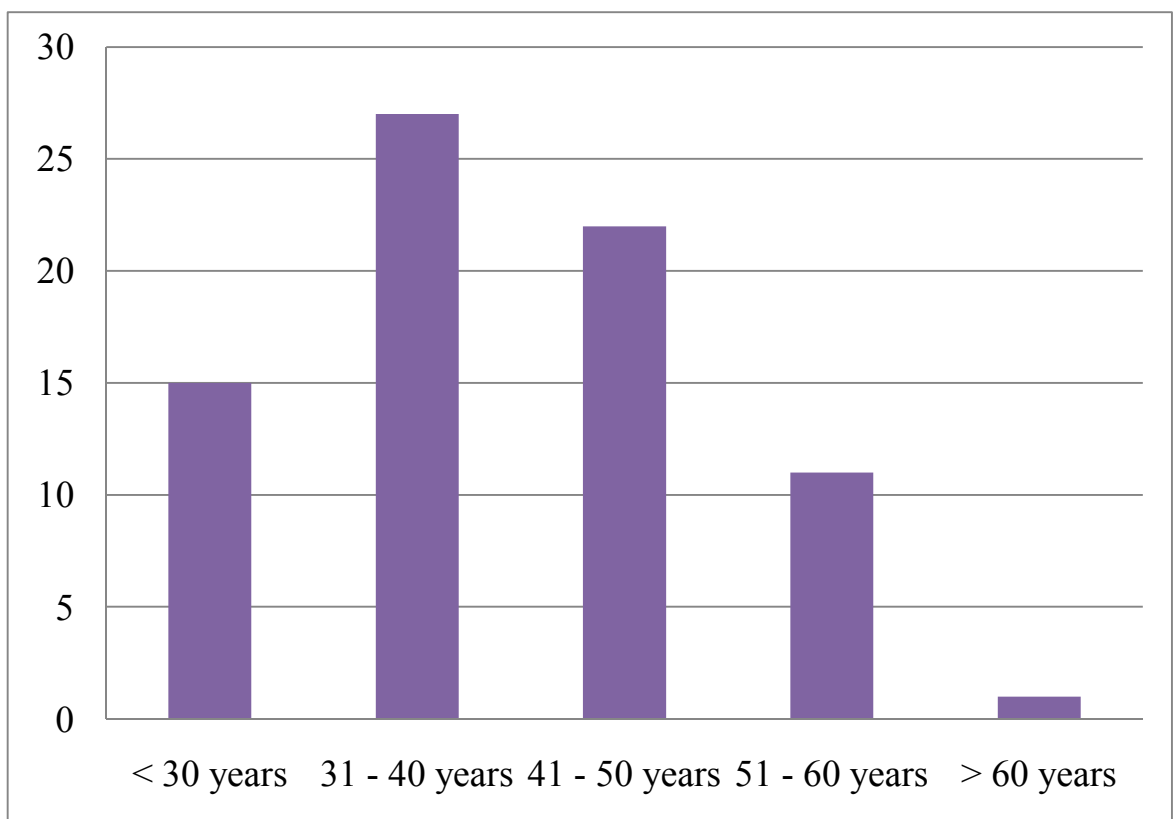
○LESS THAN 30: 15

○31 TO 40: 27

○41 TO 50: 22

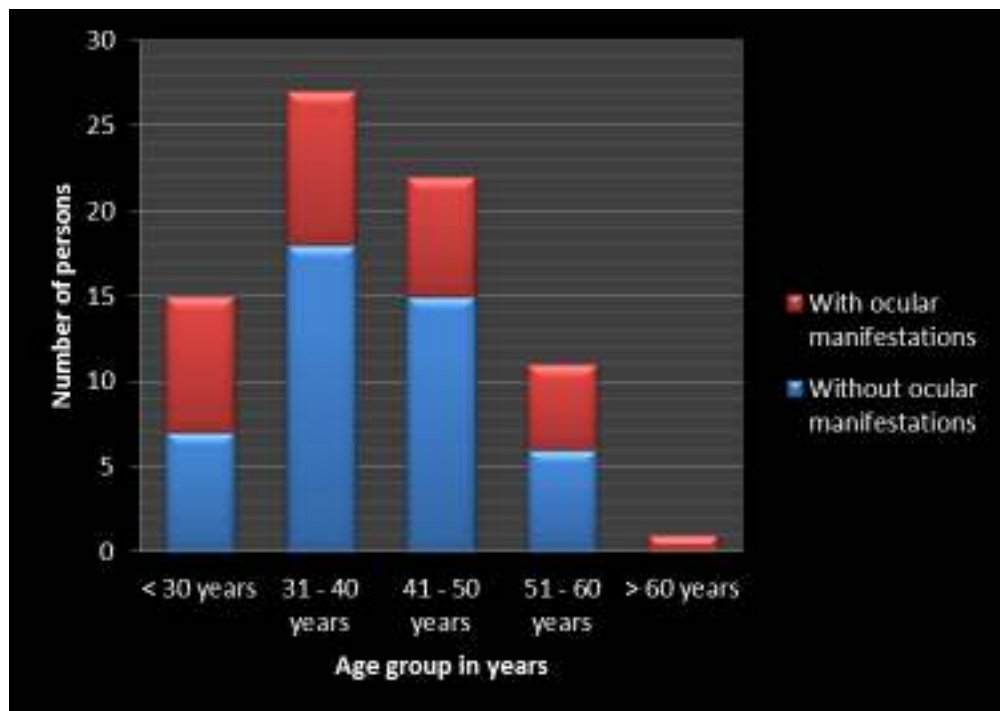
○51 TO 60: 11

○60 AND ABOVE: 1



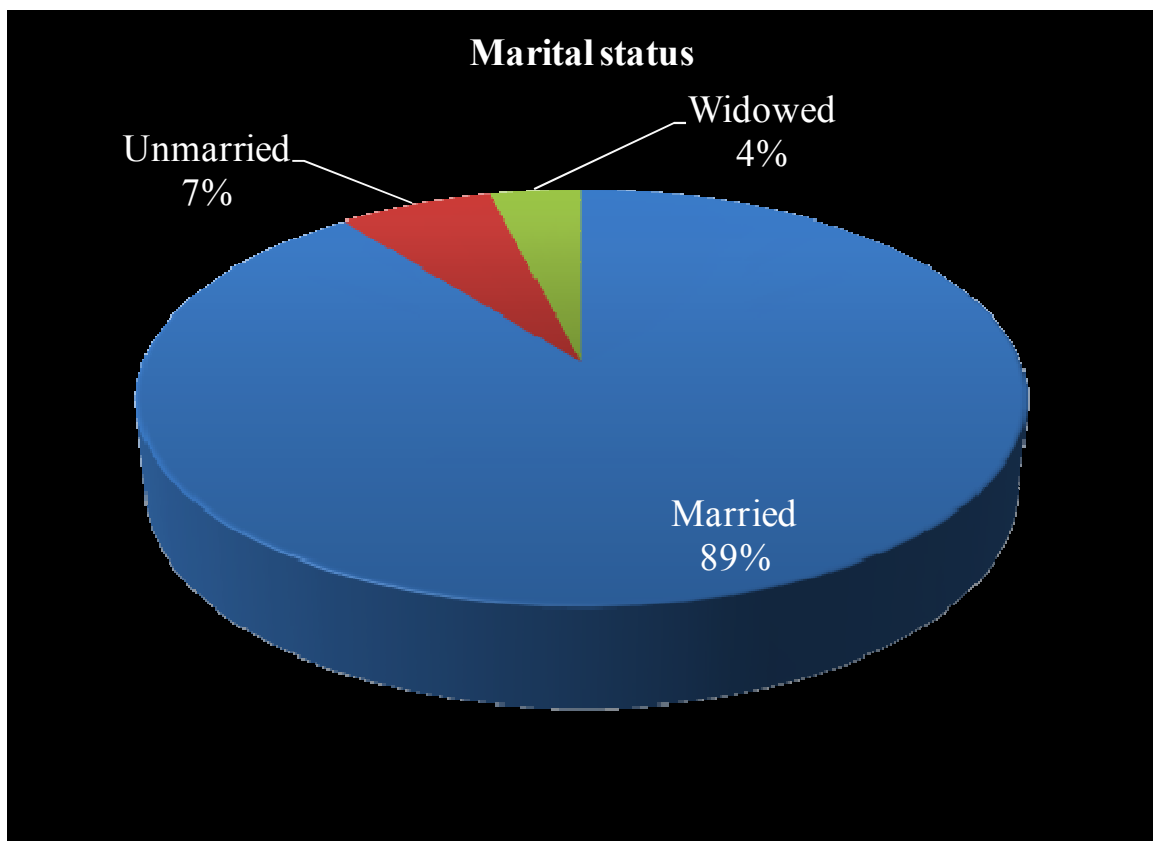
Age group	Without ocular manifestations	With ocular manifestations	Total
< 30 years	7	8	15
31 – 40 years	18	9	27
41 – 50 years	15	7	22
51 – 60 years	6	5	11
➤ 60 years	0	1	1
Total	46	30	76

The Chi-square value for the above table is 3.870 and “P” value is 0.424



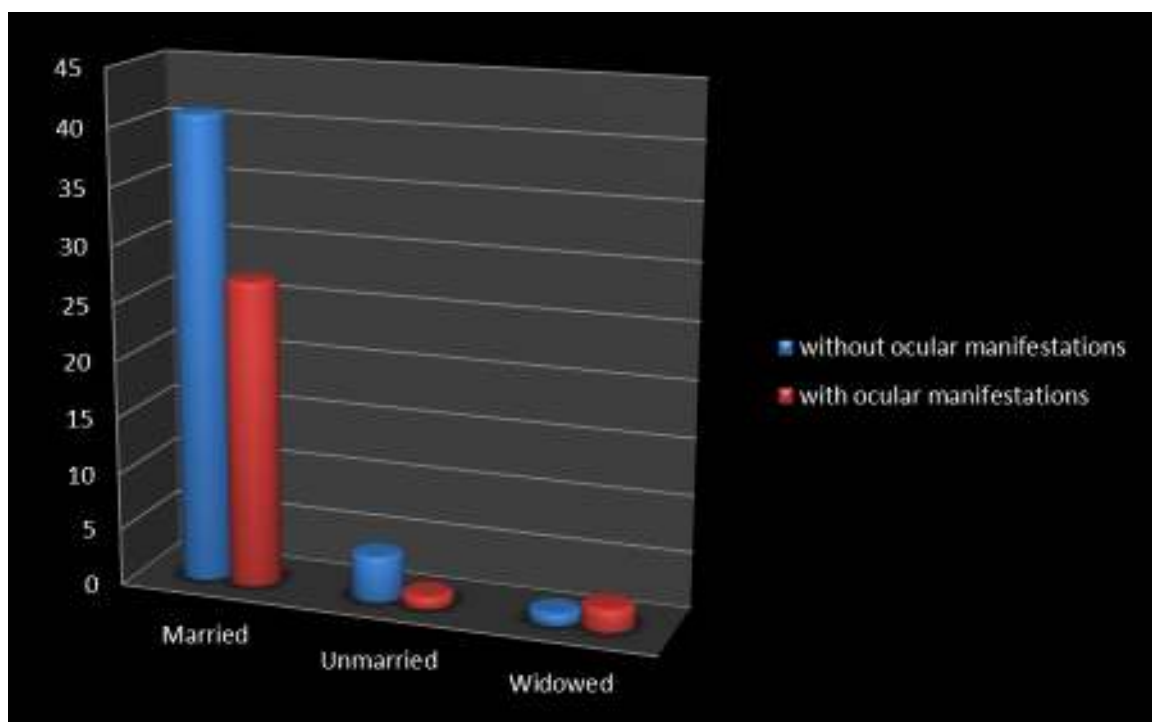
MARITAL STATUS:

- MARRIED : 68
- UNMARRIED : 5
- WIDOW : 3



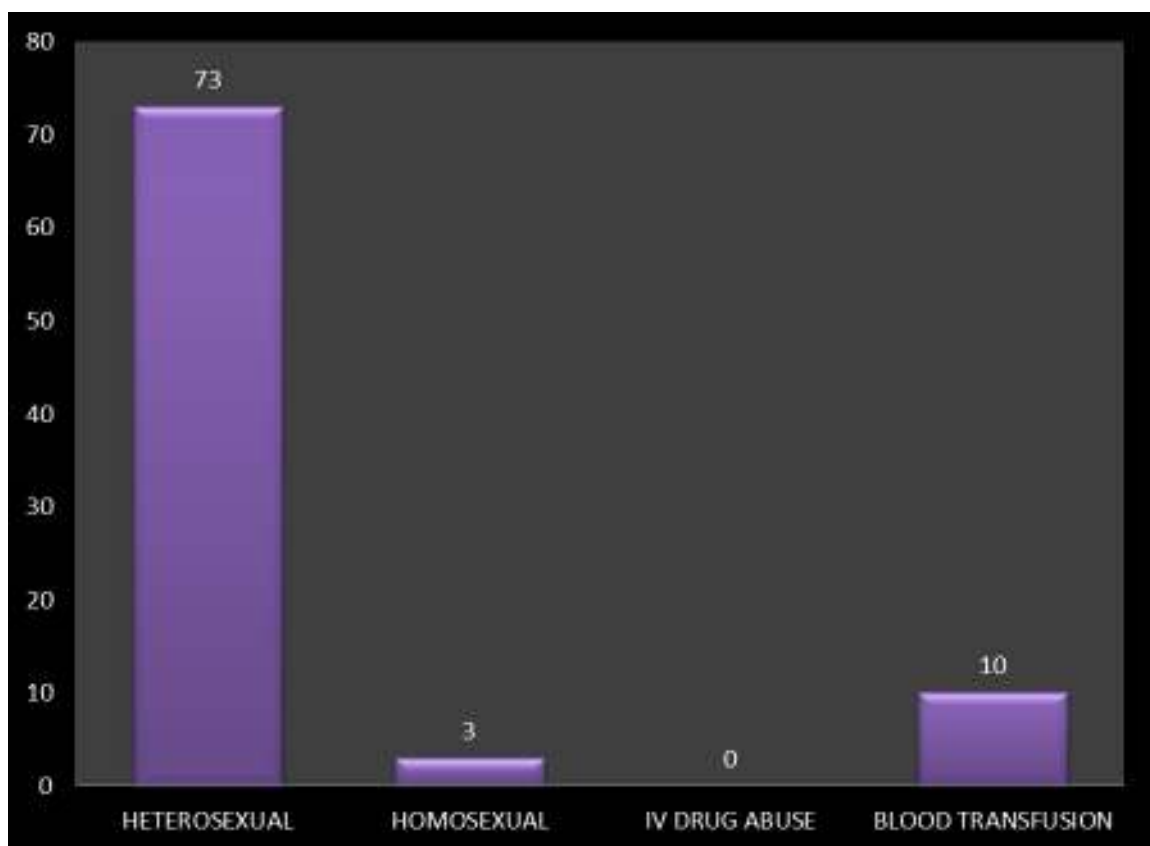
Marital status	Without ocular manifestations	With ocular manifestations	Total
Married	41	27	68
Unmarried	4	1	5
Widowed	1	2	3
Total	46	30	76

The Chi-square value for the above chart is 1.724 and the “P” value is 0.422.



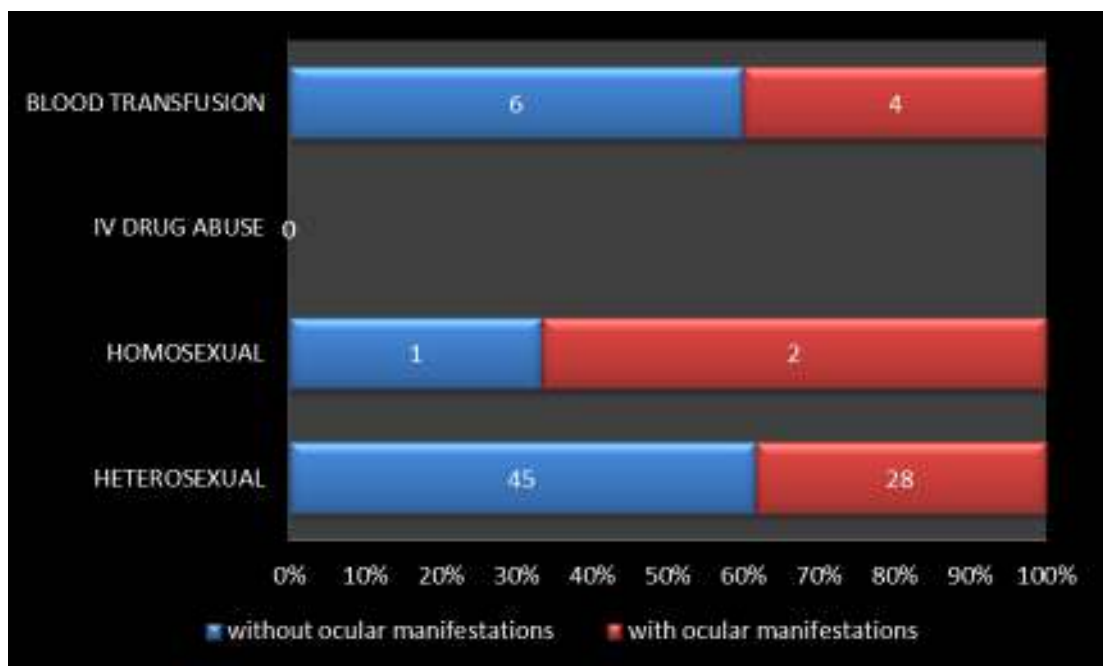
MODE OF TRANSMISSION:

- HETEROSEXUAL: 63
- HOMOSEXUAL: 3
- IV DRUG ABUSE: 0
- BLOOD TRANSFUSION: 10 (10 Patients had history of both blood transfusion and sexual promiscuity)



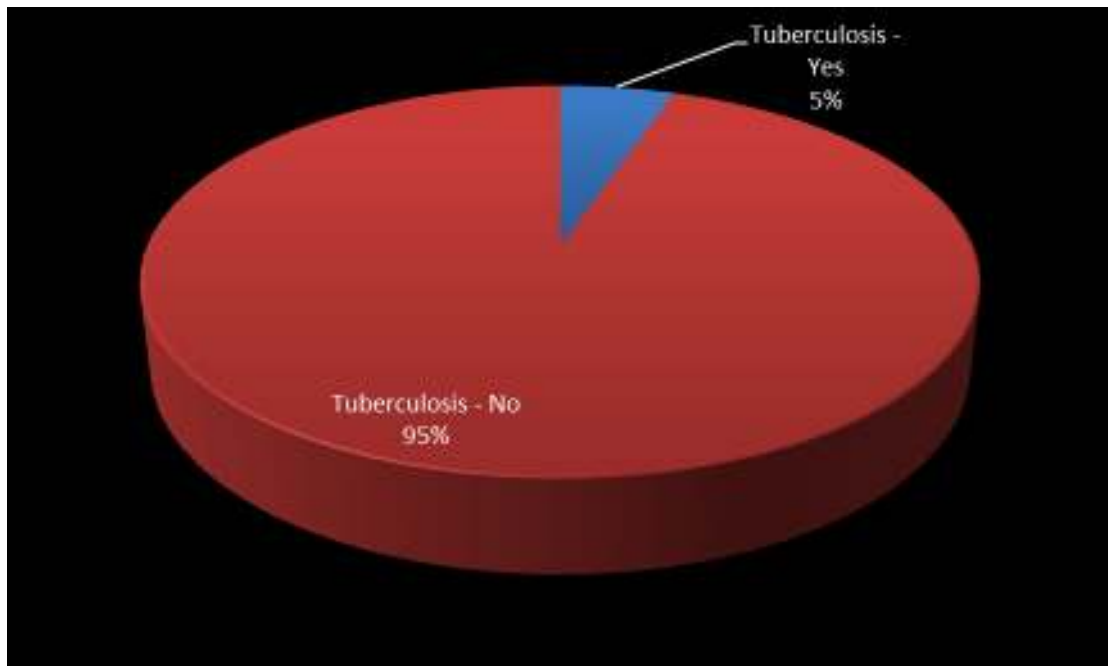
Mode of transmission	Without ocular manifestations	With ocular manifestations	Total
Heterosexual	45	28	73
Homosexual	1	2	3
IV drug abuse	0	0	0
Blood transfusion	6	4	10
	52	34	86

The chi-square value for the above test is 0.967 and the “P” value is 0.326



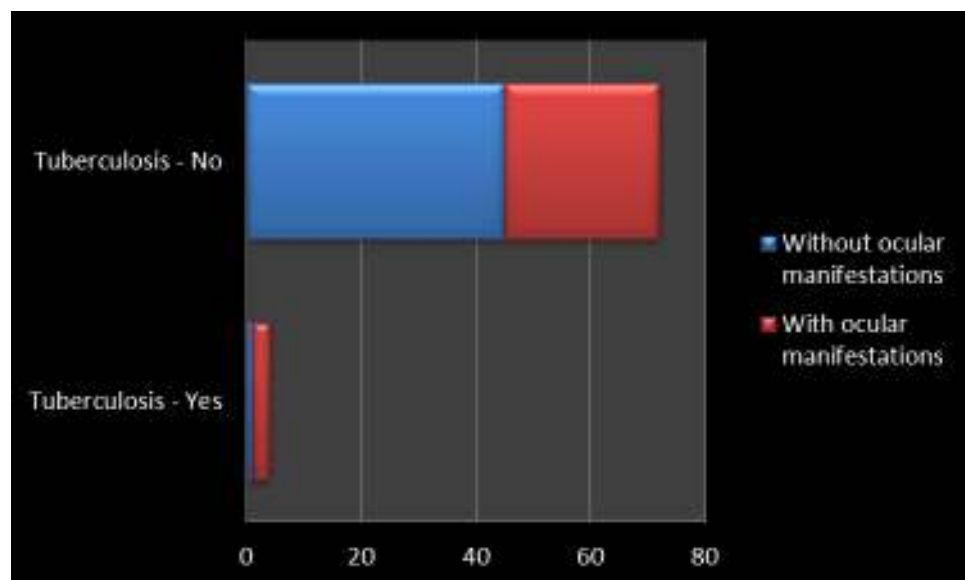
HISTORY OF TUBERCULOSIS:

- YES: 4
- NO: 72



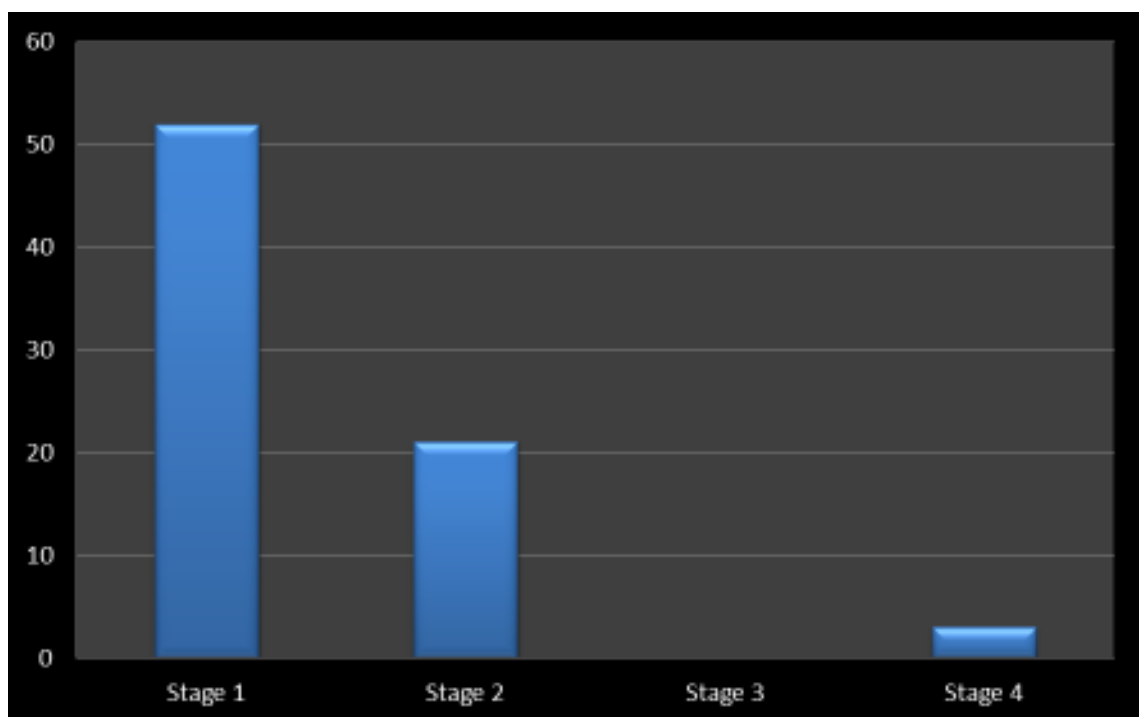
History of Tuberculosis	Without ocular manifestations	With ocular manifestations	Total
Absent	45	27	72
Present	1	3	4
Total	46	30	76

The chi-square value for the above table is 2.230 and the “P” value is 0.135



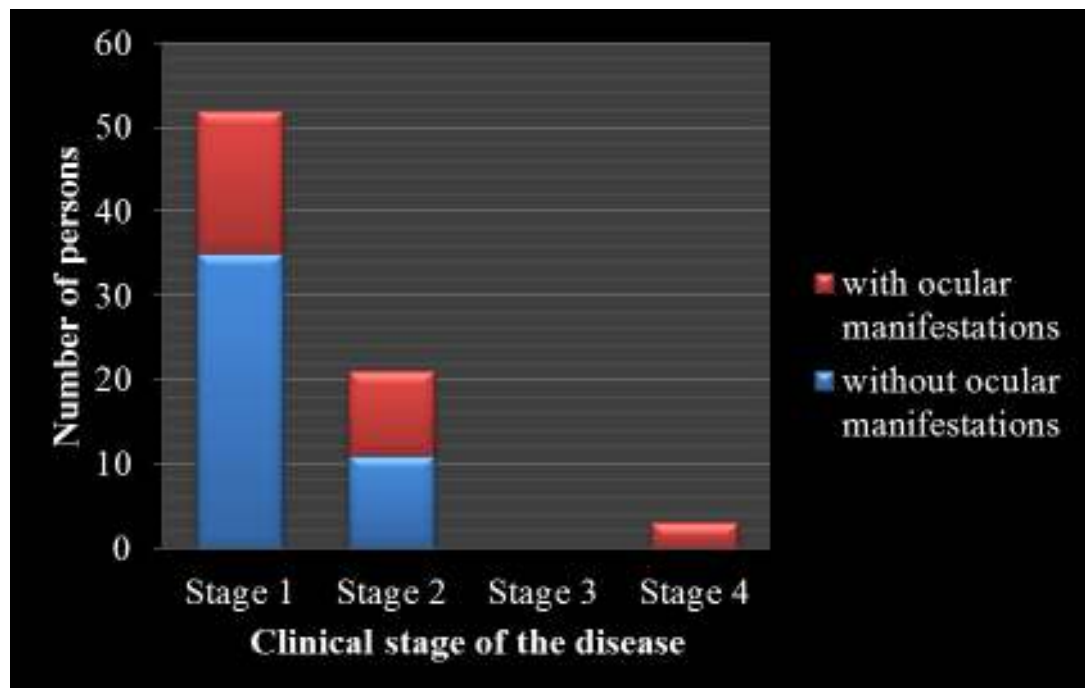
CLINICAL STAGE OF THE DISEASE:

- Stage I: 52
- Stage II: 21
- Stage III: 0
- Stage IV: 3



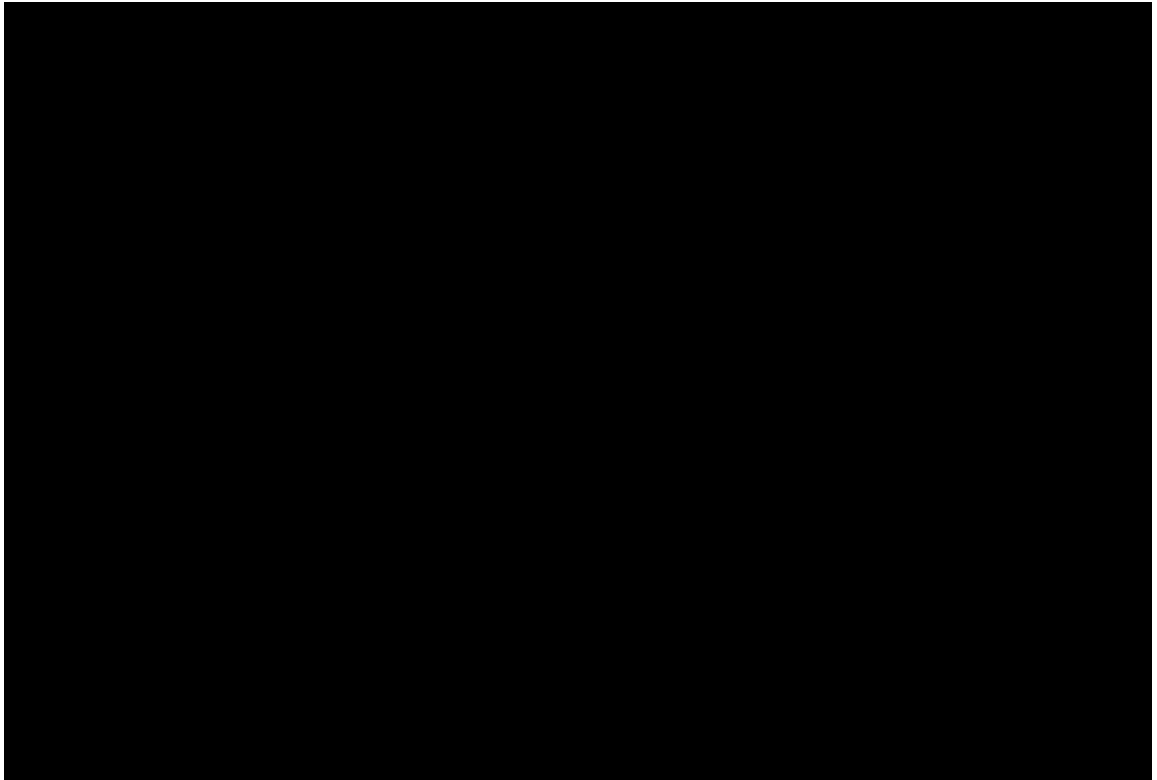
Clinical stage of the disease	Without ocular manifestations	With ocular manifestations	Total
Stage I	35	17	52
Stage II	11	10	21
Stage III	0	0	0
Stage IV	0	3	3
Total	46	30	76

The chi-square value for the above table is 6.184 and the “P” value is 0.045



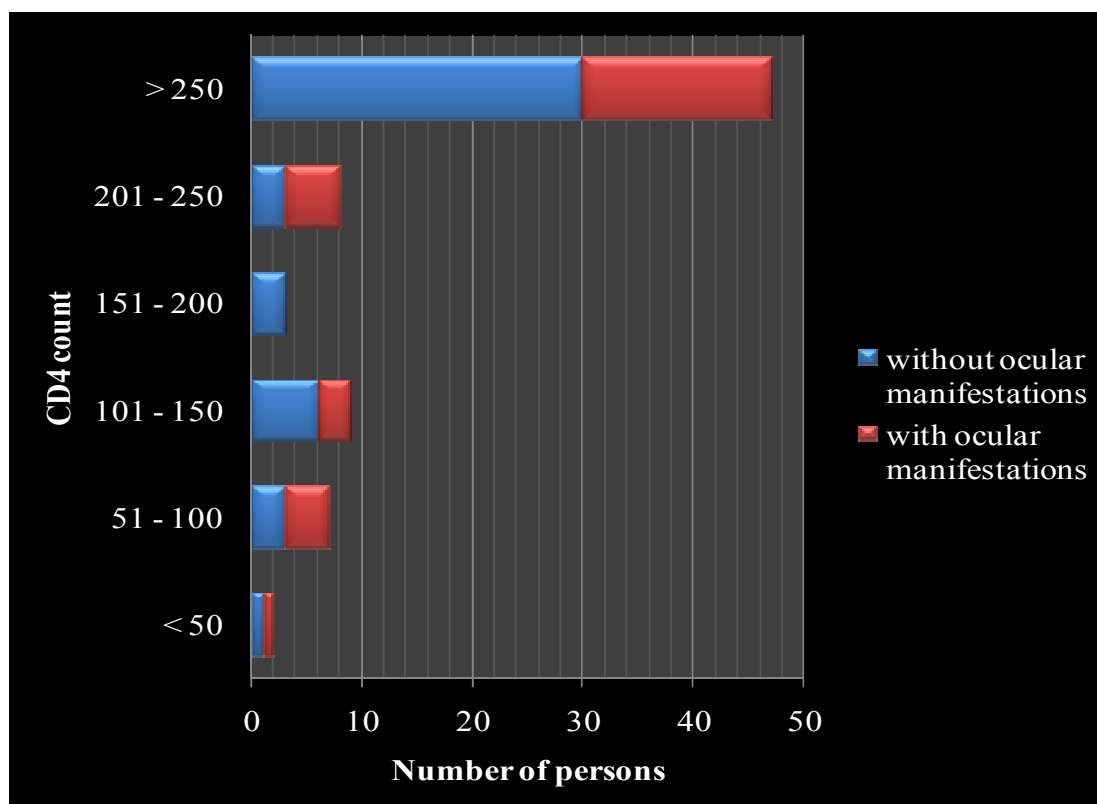
CD4+ COUNT:

- <50: 2
- 51 TO 100: 7
- 101 TO 150: 9
- 151 TO 200: 3
- 201 TO 250: 8
- >250: 47



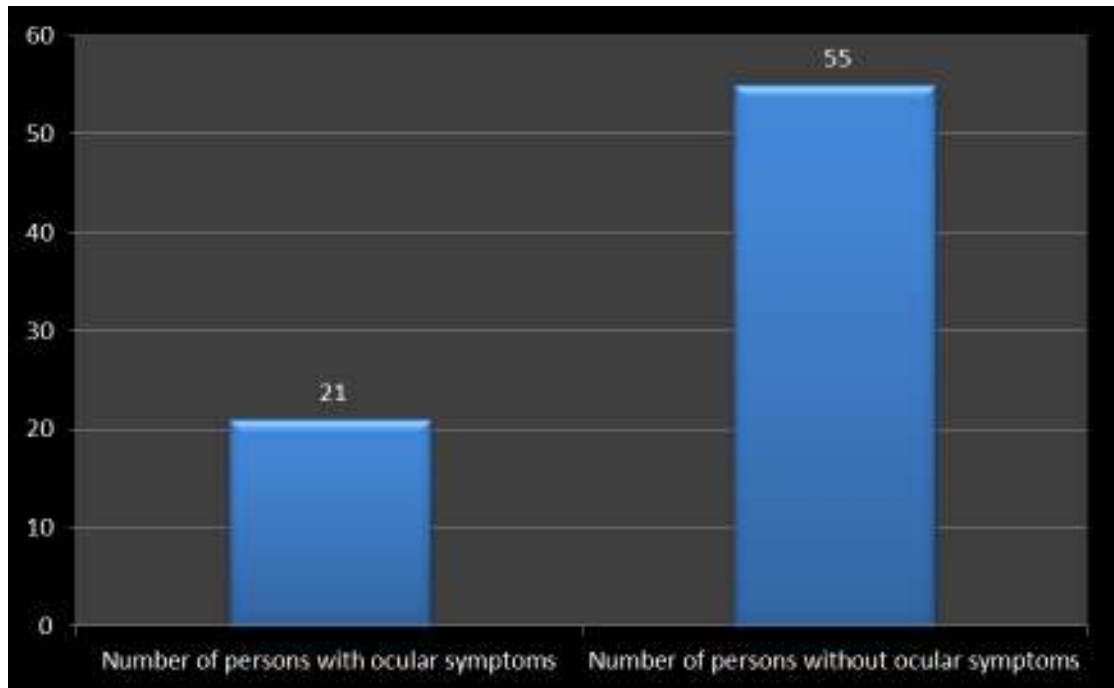
CD4 count	Without ocular manifestations	With ocular manifestations	Total
< 50	1	1	2
51 - 100	3	4	7
101 - 150	6	3	9
151 - 200	3	0	3
201 - 250	3	5	8
➤ 250	30	17	47
Total	46	30	76

The chi-square value for the above table is 5.096 and the “P” value is 0.404



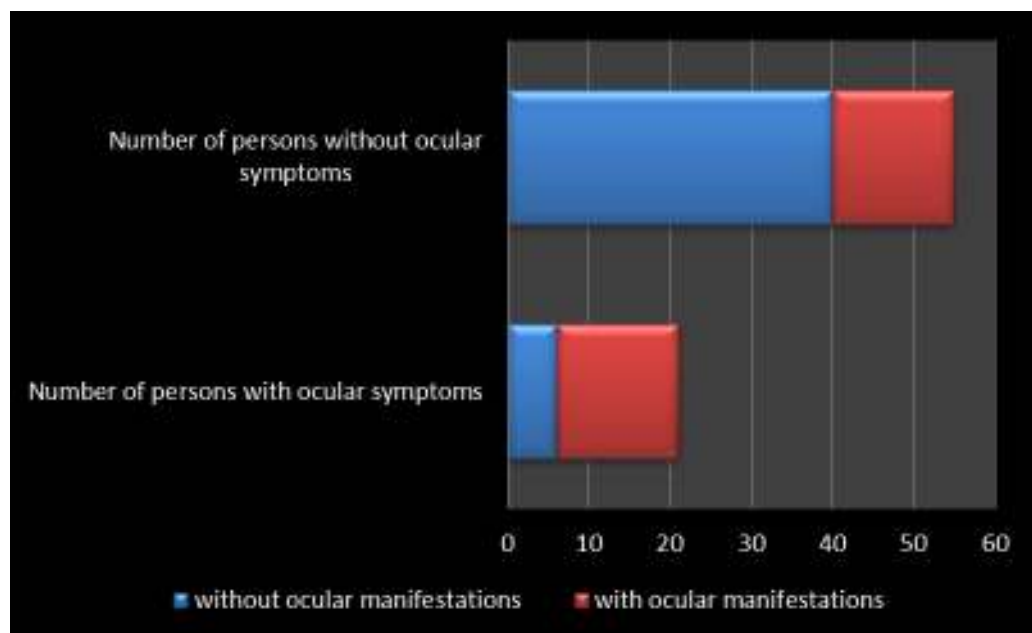
HISTORY OF OCULAR SYMPTOMS:

- YES: 21
- NO: 55



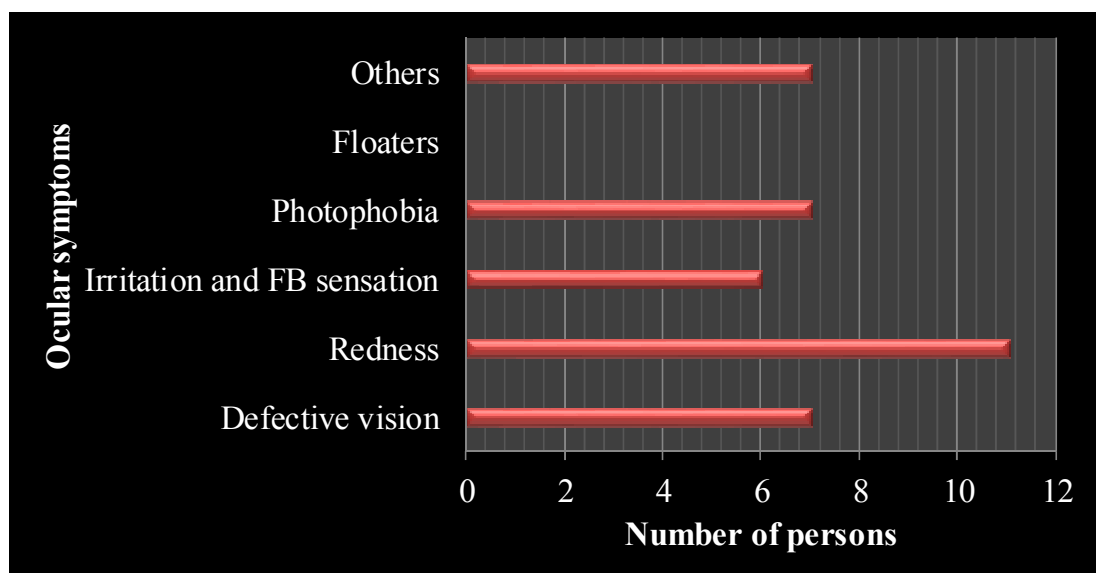
Presence of ocular symptoms	Without ocular manifestations	With ocular manifestations	Total
Yes	6	15	21
No	40	15	55
Total	46	30	76

The chi-square value for the above table is 12.404 and the “P” value is 0.000



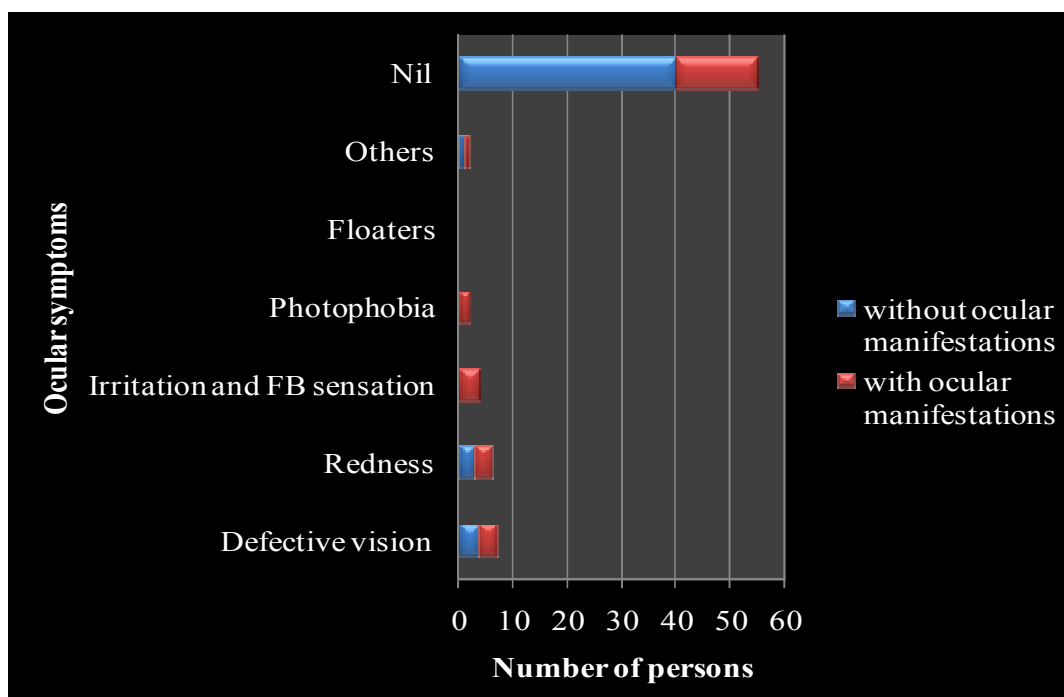
TYPES OF OCULAR SYMPTOMS:

- DEFECTIVE VISION: 7
- REDNESS: 11
- IRRITATION & FB SENSATION: 6
- PHOTOPHOBIA: 7
- FLOATERS: 0
- OTHERS: 7



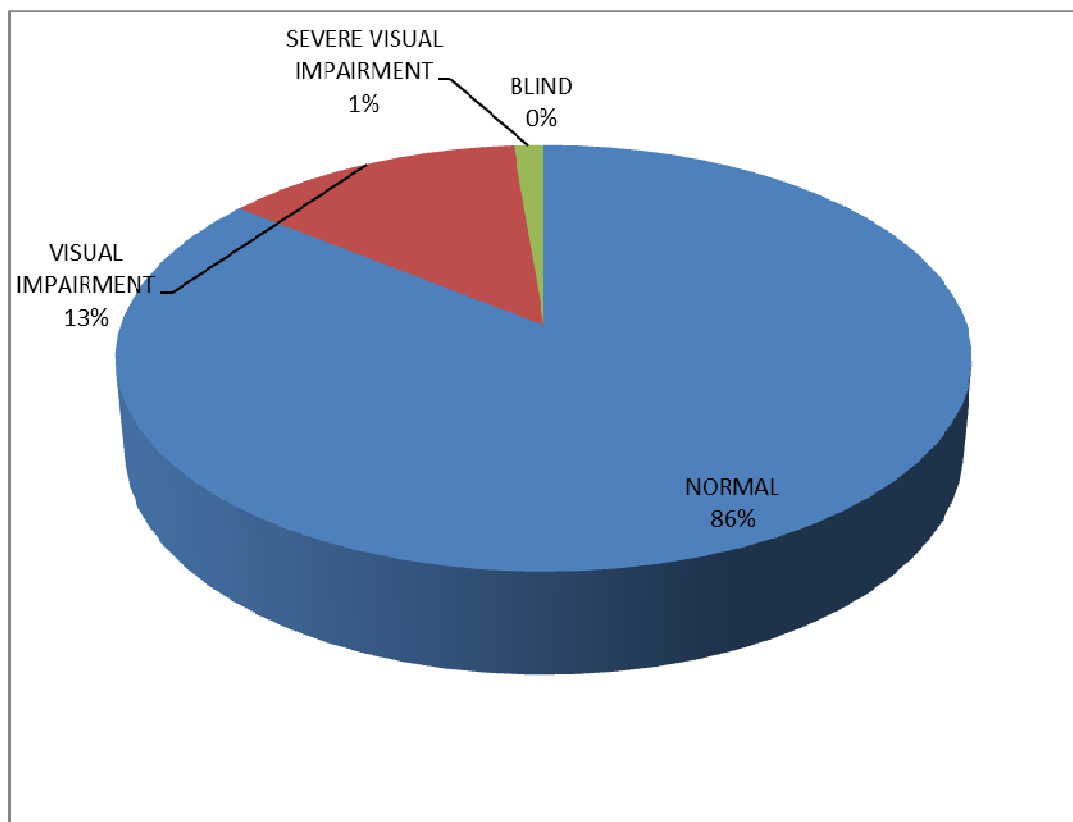
Ocular symptoms	Without ocular manifestations	With ocular manifestations	Total
Nil	40	15	55
Defective vision	2	5	7
Redness	3	3	6
Irritation & FB Sensation	0	4	4
Photophobia	0	2	2
Floater	0	0	0
Others	1	1	2
Total	46	30	76

The chi-square value for the above table is 18.082 and the “P” value is 0.012



VISUAL ACUITY – BOTH EYES:

- NORMAL (6/6 – 6/18 in the better eye) :65
- VISUAL IMPAIRMENT(<6/18 – 6/60 in better eye): - 10
- SEVERE VISUAL IMPAIRMENT(<6/60 – 3/60 in the better eye) – 1
- BLIND (<3/60 in the better eye)– NIL

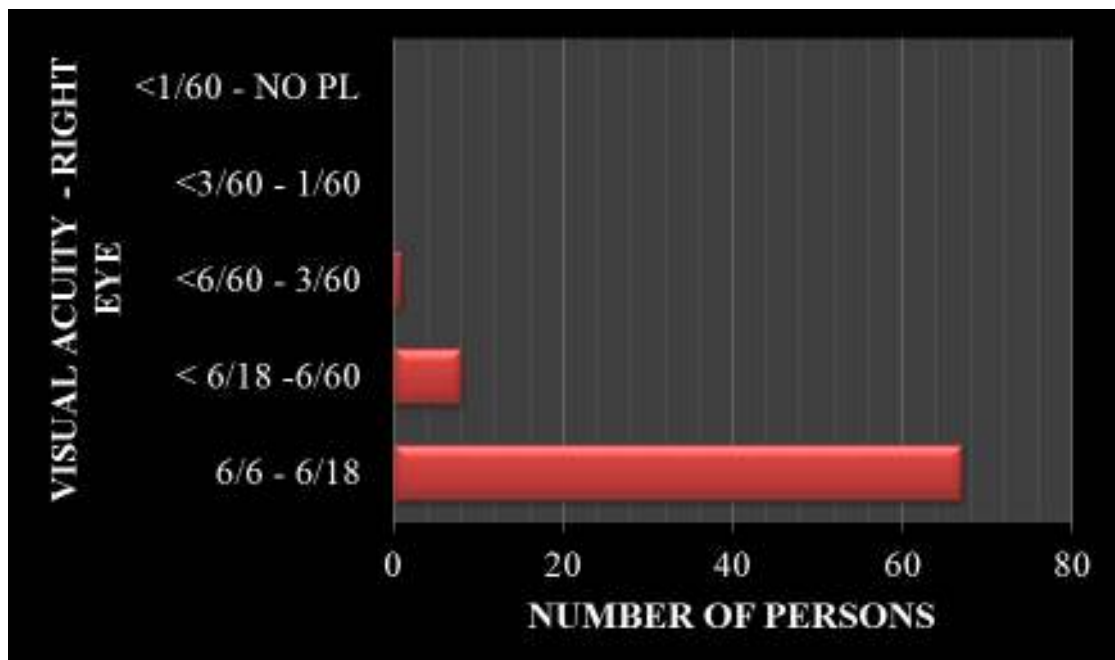


Visual acuity – both eyes	Without ocular manifestations	With ocular manifestations	Total
Normal 6/6 – 6/18 in the better eye	40	25	65
Visual impairment <6/18 – 6/60 in the better eye	5	5	10
Severe visual impairment <6/60 – 3/60 in the better eye	1	0	1
Blind <3/60 – 1/60 in the better eye	0	0	0
Blind <1/60 – NO PL	0	0	0
Total	46	30	76

The chi-square value for the above table is 1.144 and the “p” value is 0.464

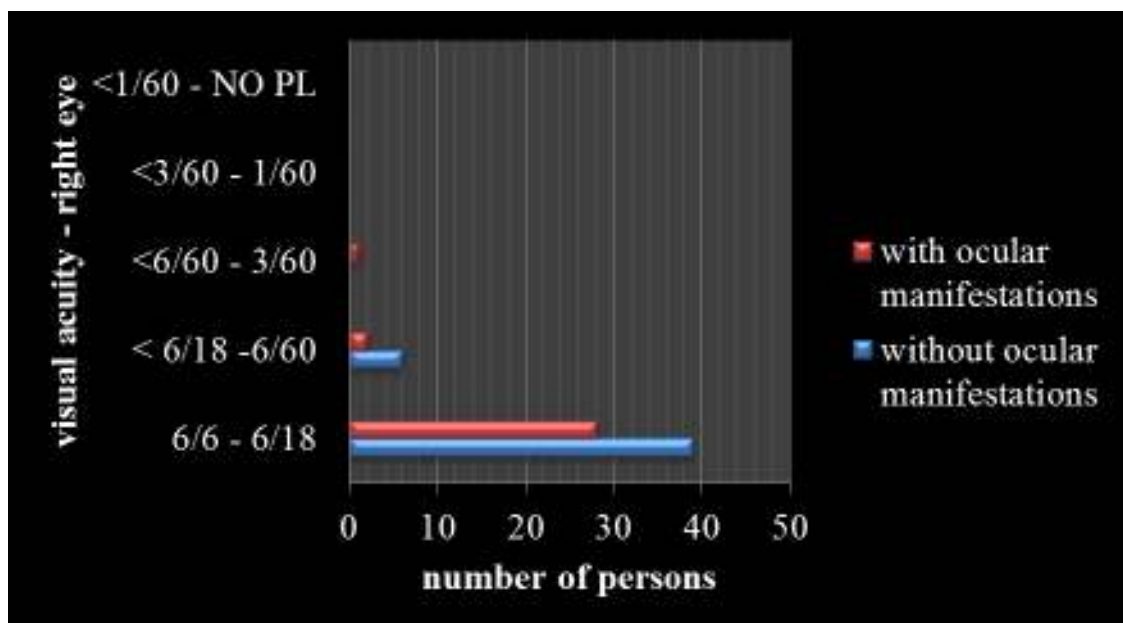
VISUAL ACUITY - RIGHT EYE:

- 6/6 – 6/18: 67
- < 6/18 – 6/60: 8
- < 6/60 – 3/60: 1
- < 3/60 – 1/60: 0
- <1/60 – NO PL: 0



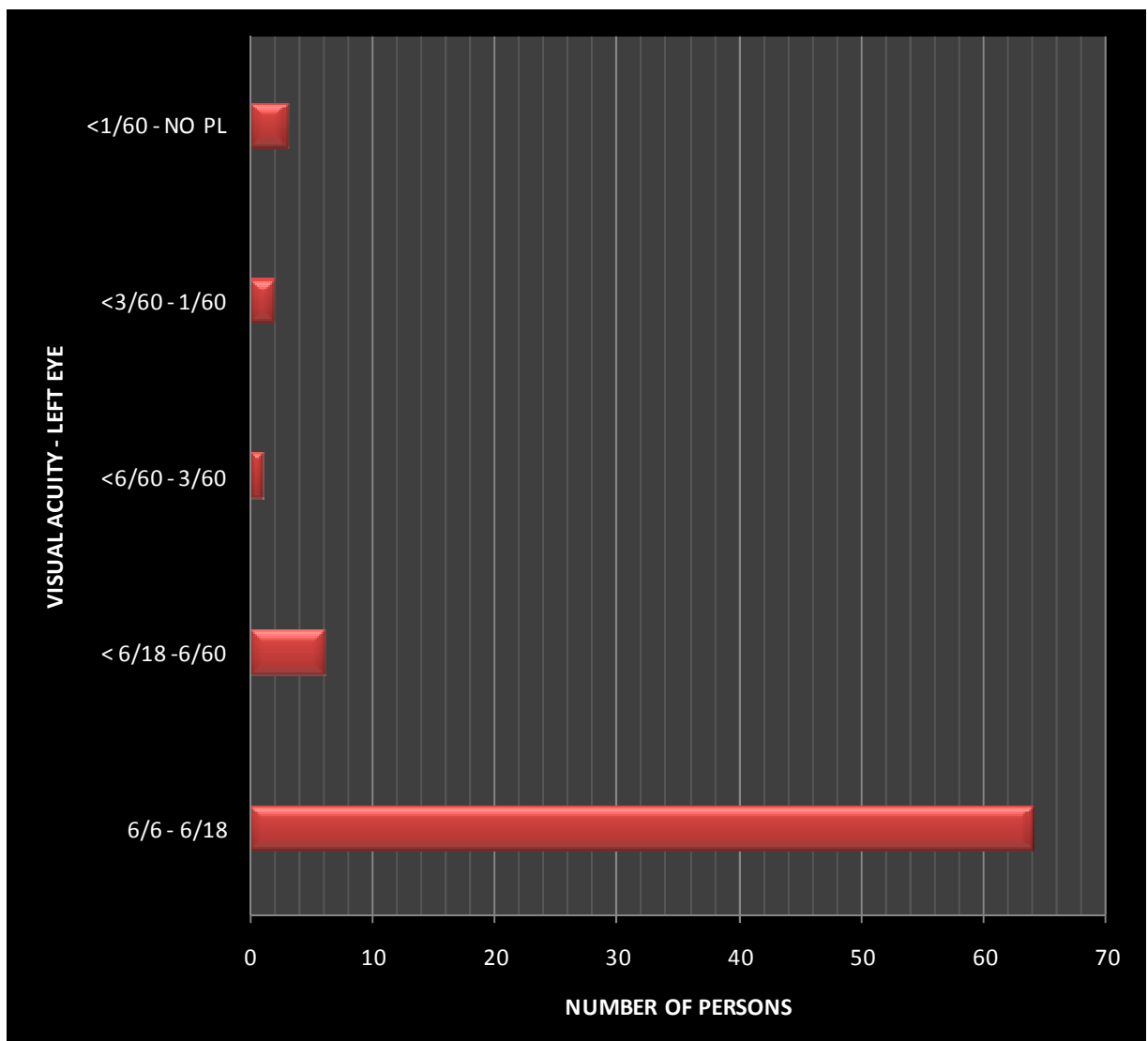
Visual acuity – Right eye	Without ocular manifestations	With ocular manifestations	Total
6/6 – 6/18	39	28	67
<6/18 – 6/60	6	2	8
<6/60 – 3/60	0	1	1
<3/60 – 1/60	0	0	0
<1/60 – NO PL	0	0	0
TOTAL	46	30	76

The chi-square value for the above chart is 1.504 and the “P” Value is 0.471



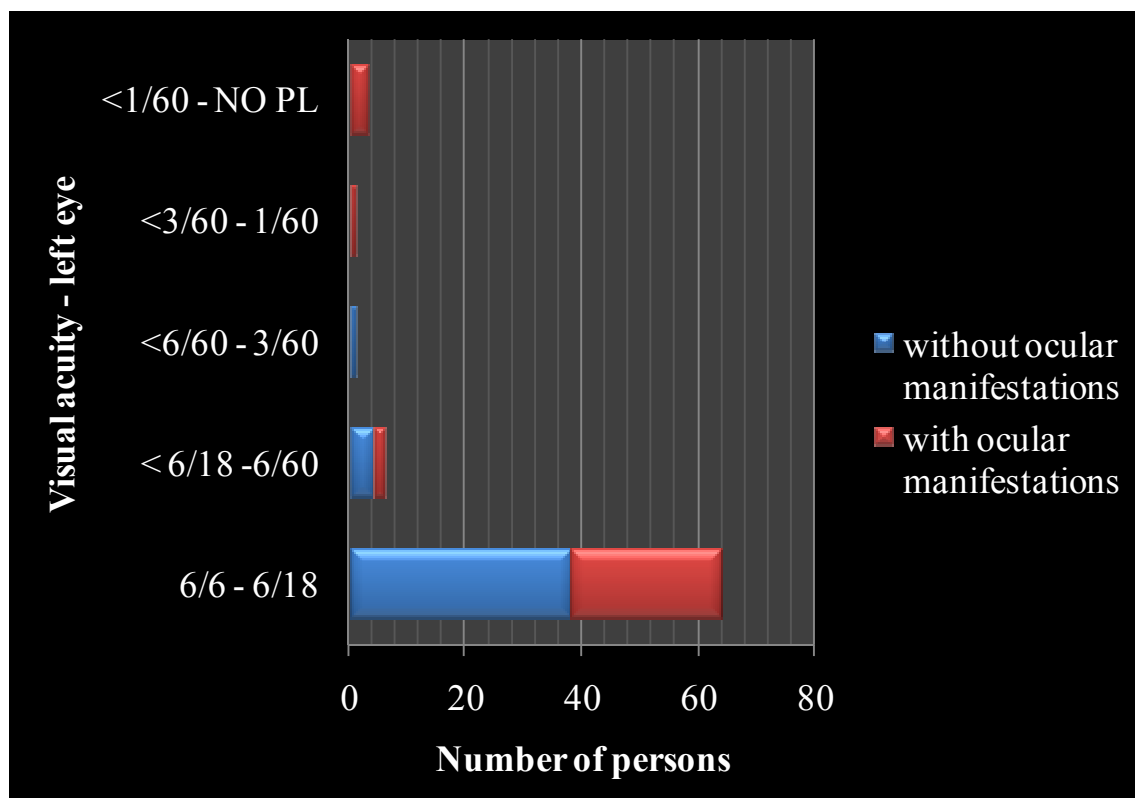
VISUAL ACUITY - LEFT EYE:

- 6/6 – 6/18: 64
- <6/18 – 6/60: 6
- <6/60 – 3/60: 1
- <3/60 – 1/60: 2
- <1/60 – NO PL: 3



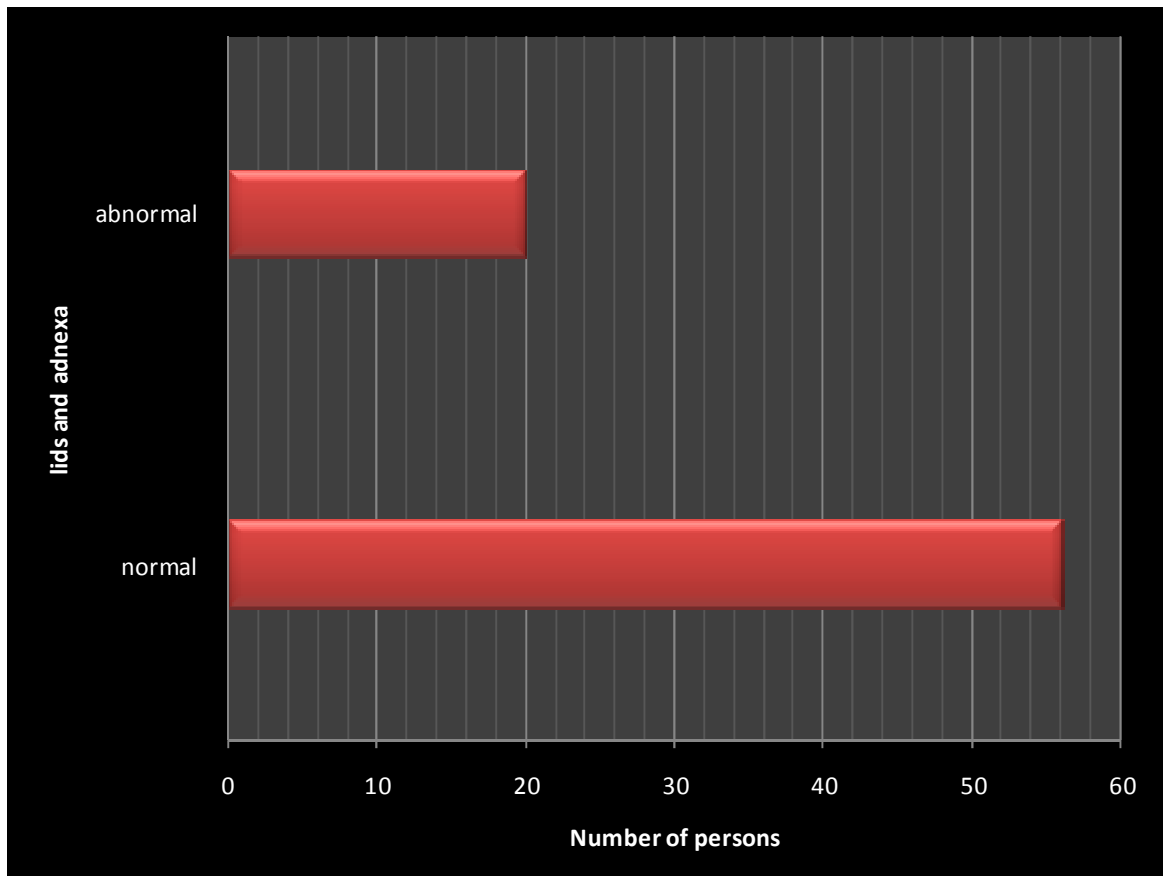
Visual acuity – left eye	Without ocular manifestations	With ocular manifestations	Total
6/6 – 6/18	38	26	64
<6/18 – 6/60	4	2	6
<6/60 – 3/60	1	0	1
<3/60 – 1/60	0	2	2
<1/60 – NO PL	0	3	3
Total	46	30	76

The chi-square value for the above table is 5.108 and the “P” value is 0.276



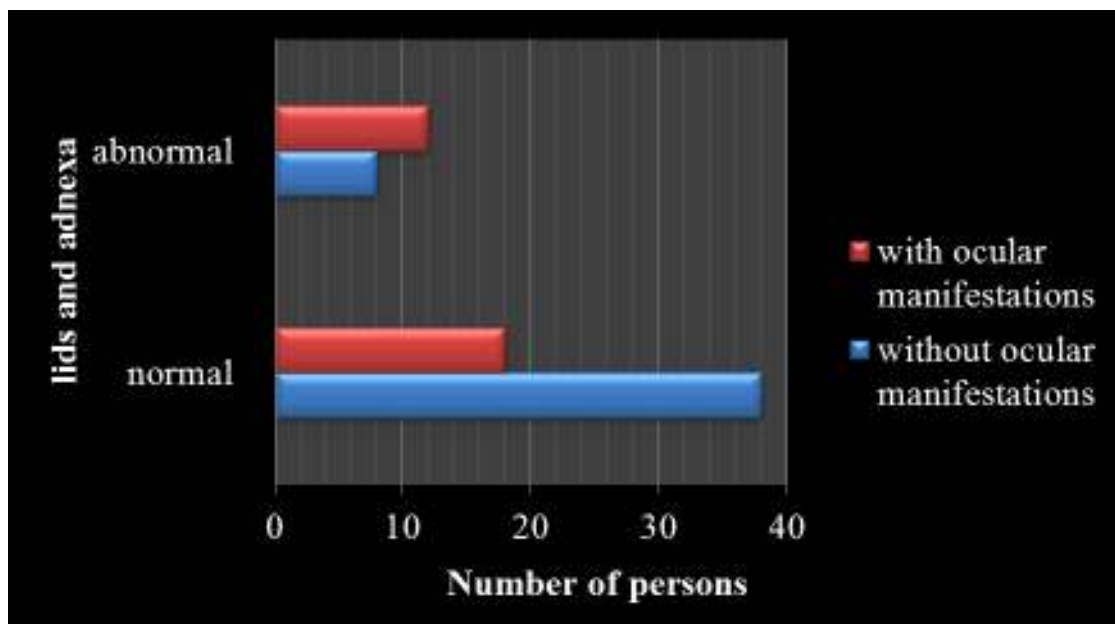
LIDS AND ADNEXA:

- NORMAL : 56
- ABNORMAL: 20



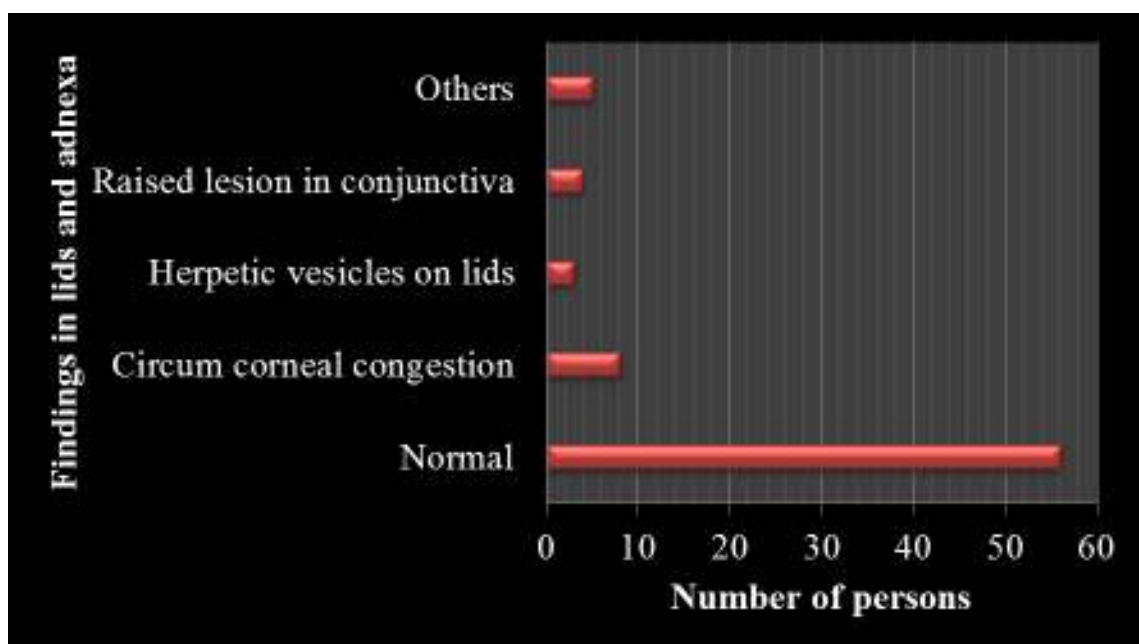
Lids and adnexa	Without ocular manifestations	With ocular manifestations	Total
Normal	38	18	56
Abnormal	8	12	20
Total	46	30	76

The chi-square value for the above table is 4.787 and the “P” value is 0.029



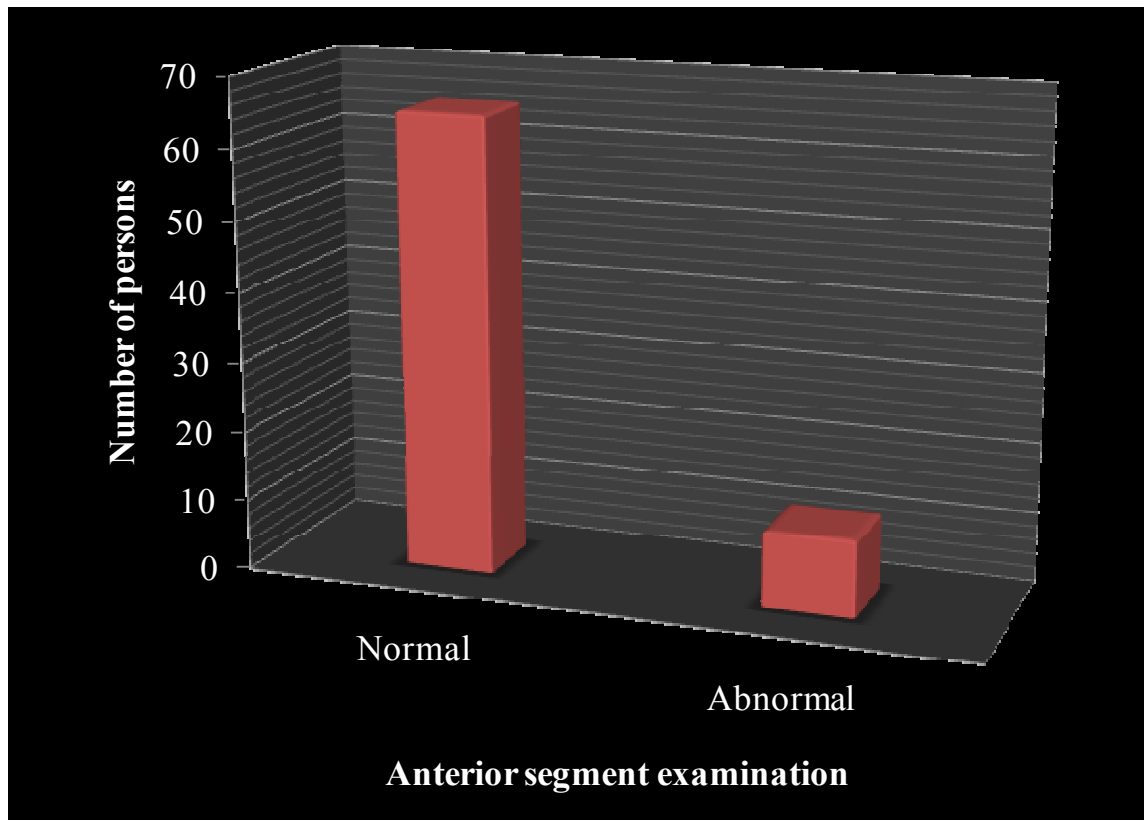
FINDINGS IN LIDS AND ADNEXA:

- Normal : 56
- Herpetic lesions on lids: 3
- Circum corneal congestion: 8
- Raised lesion in conjunctiva: 4
- Others : 5



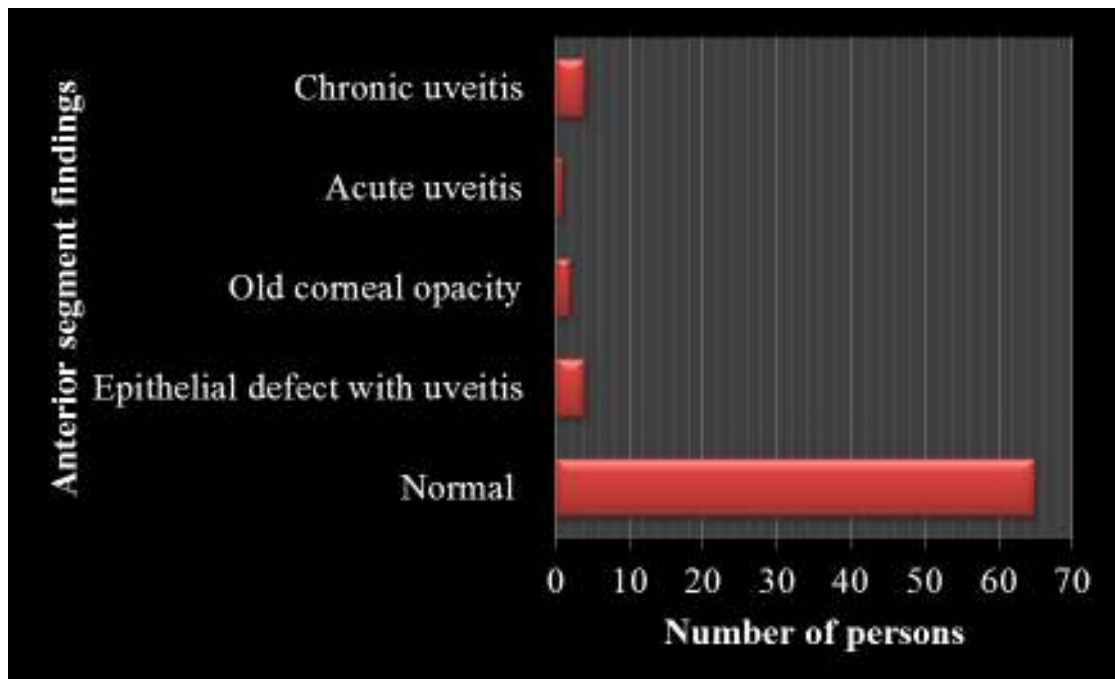
ANTERIOR SEGMENT BY SLIT LAMP EXAMINATION:

- NORMAL: 65
- FINDINGS PRESENT: 11



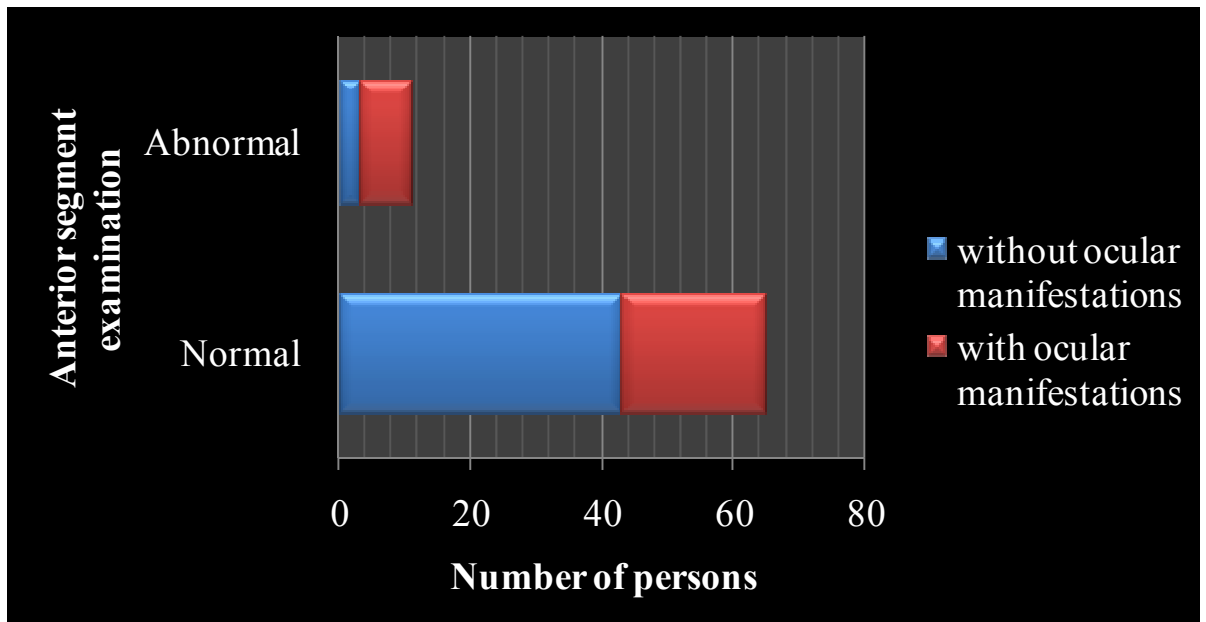
ANTERIOR SEGMENT FINDINGS:

- Normal : 65
- Epithelial defect with uveitis : 4
- Old corneal opacity : 2
- Signs of active uveitis : 1
- Signs of chronic uveitis : 4



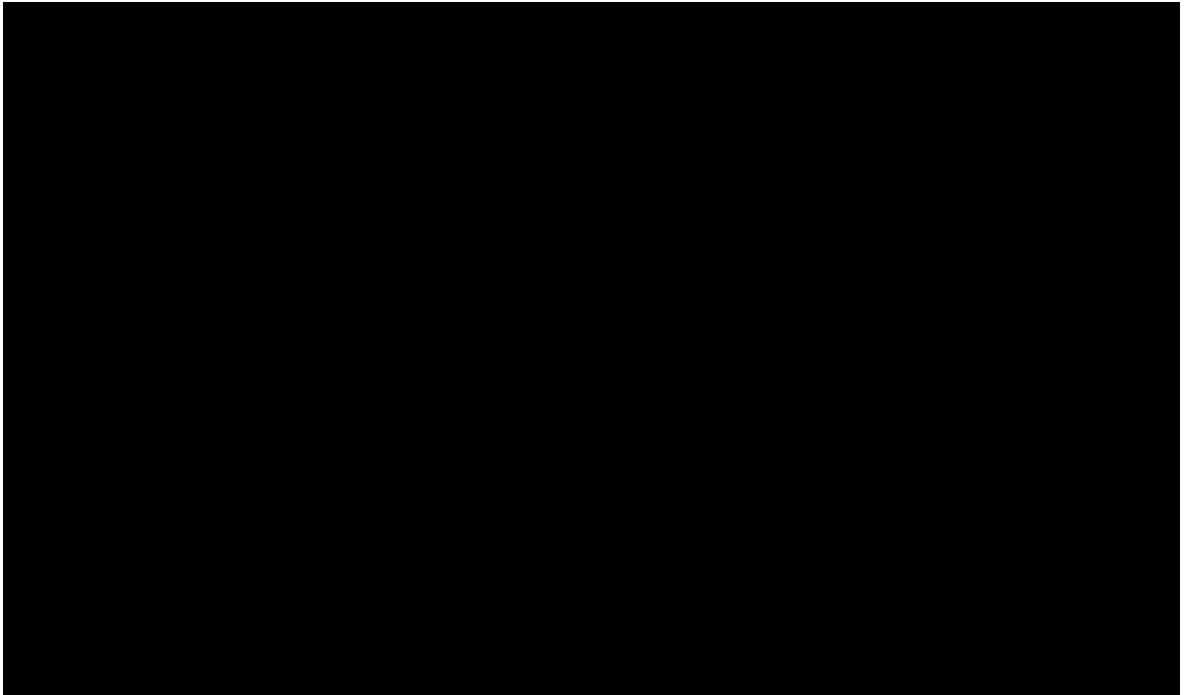
Anterior segment examination	Without ocular manifestations	With ocular manifestations	Total
Normal	43	22	65
Abnormal	3	8	11
Total	46	30	76

The chi-square value for the above table is 4.491 and the “P” value is 0.034



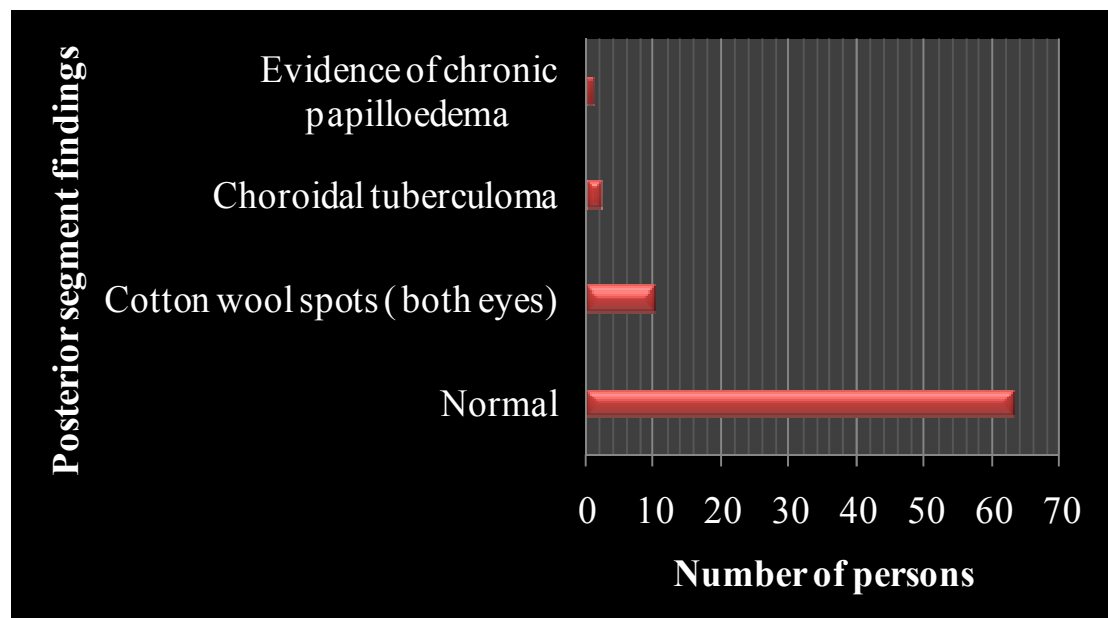
POSTERIOR SEGMENT:

- FINDINGS PRESENT: 13
- NORMAL FUNDUS: 63



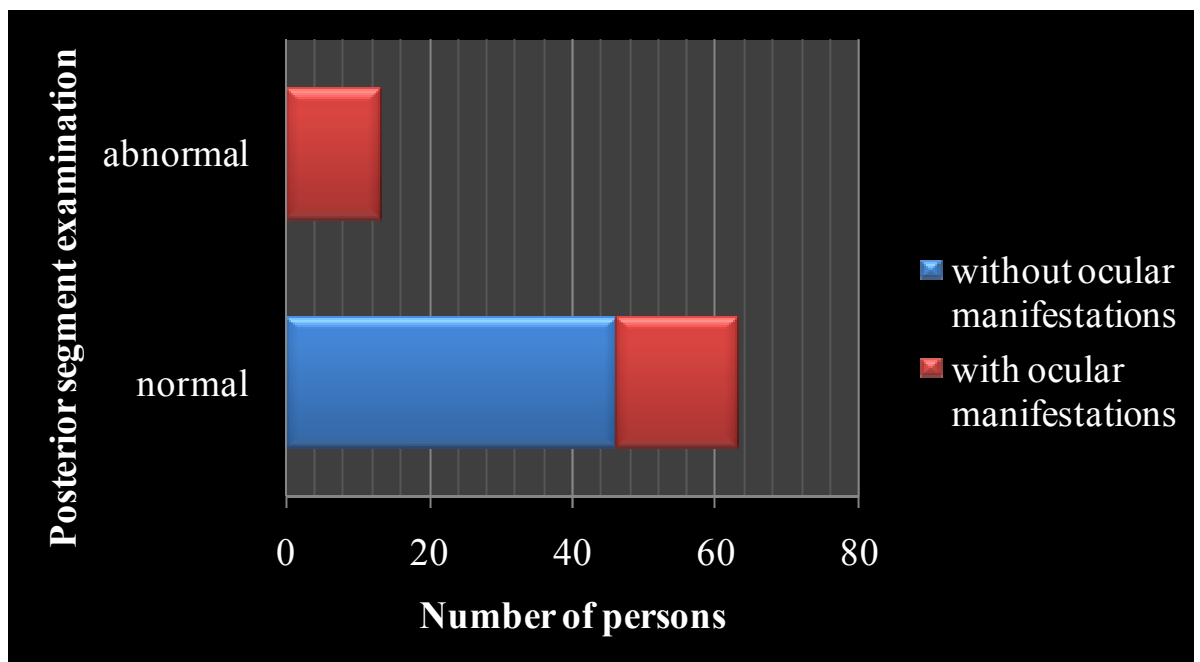
POSTERIOR SEGMENT FINDINGS:

- COTTON WOOL SPOTS: 10
- CHOROIDAL GRANULOMA (TUBERCULOMA): 2
- DISC EDEMA WITH HEMORRHAGES AND EXUDATES: 1
- NORMAL FUNDUS : 63



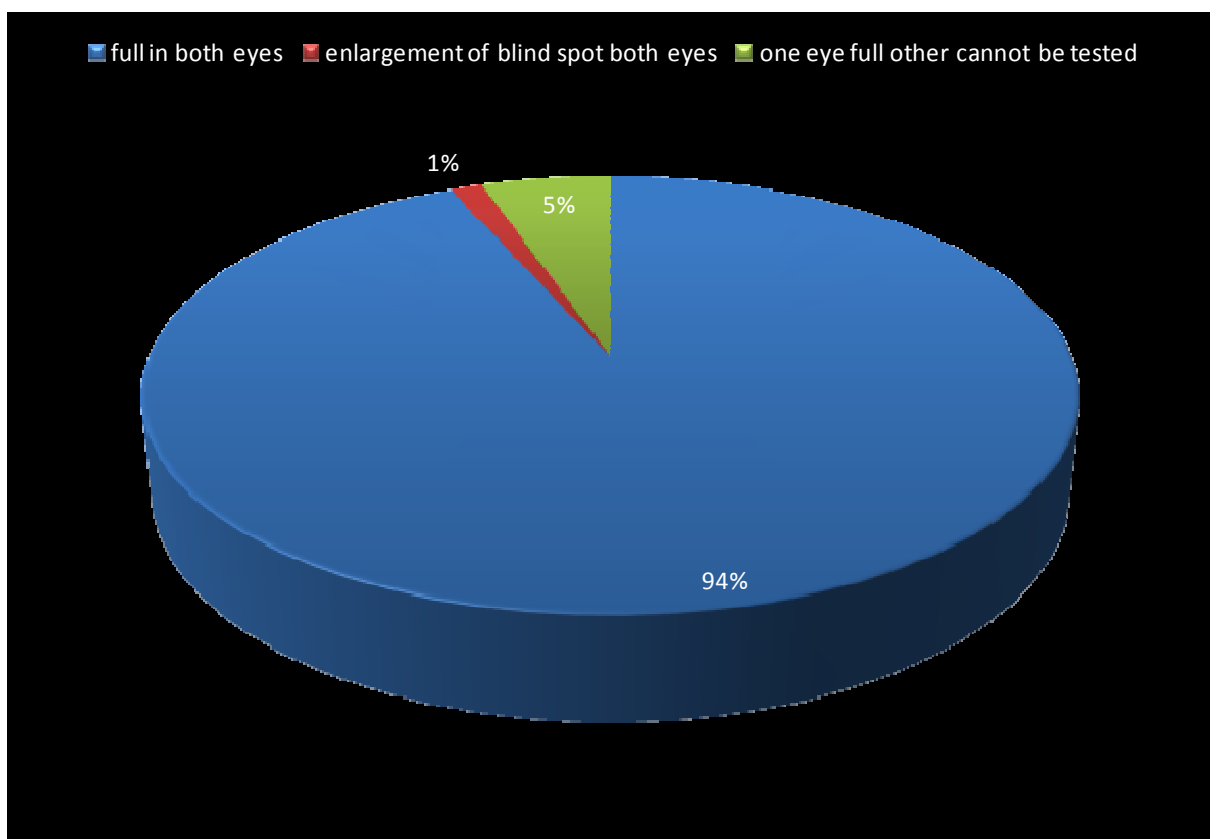
Posterior segment examination	Without ocular manifestations	With ocular manifestations	Total
Normal	46	17	63
Abnormal	0	13	13
Total	46	30	76

The chi - square value for the above table is 24.047 and the “P” value is 0.000



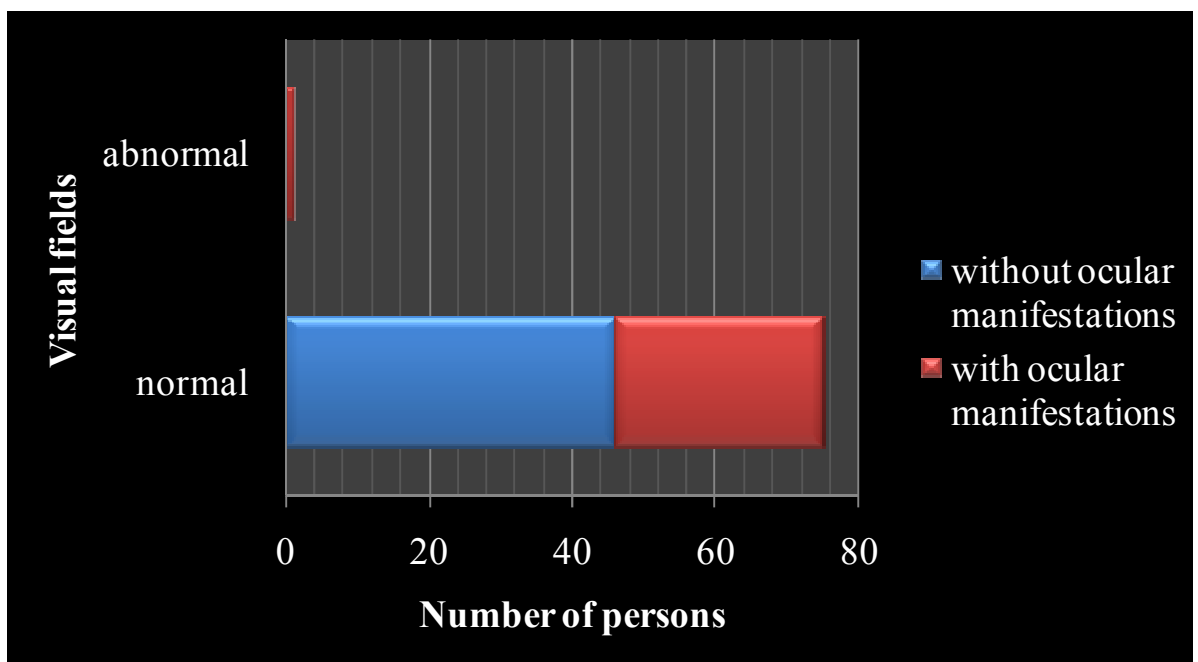
VISUAL FIELDS:

- FULL IN BOTH EYES: 71
- ENLARGEMENT OF BLIND SPOT BOTH EYES: 1
- ONE EYE FULL OTHER EYE CANNOT BE TESTED: 4



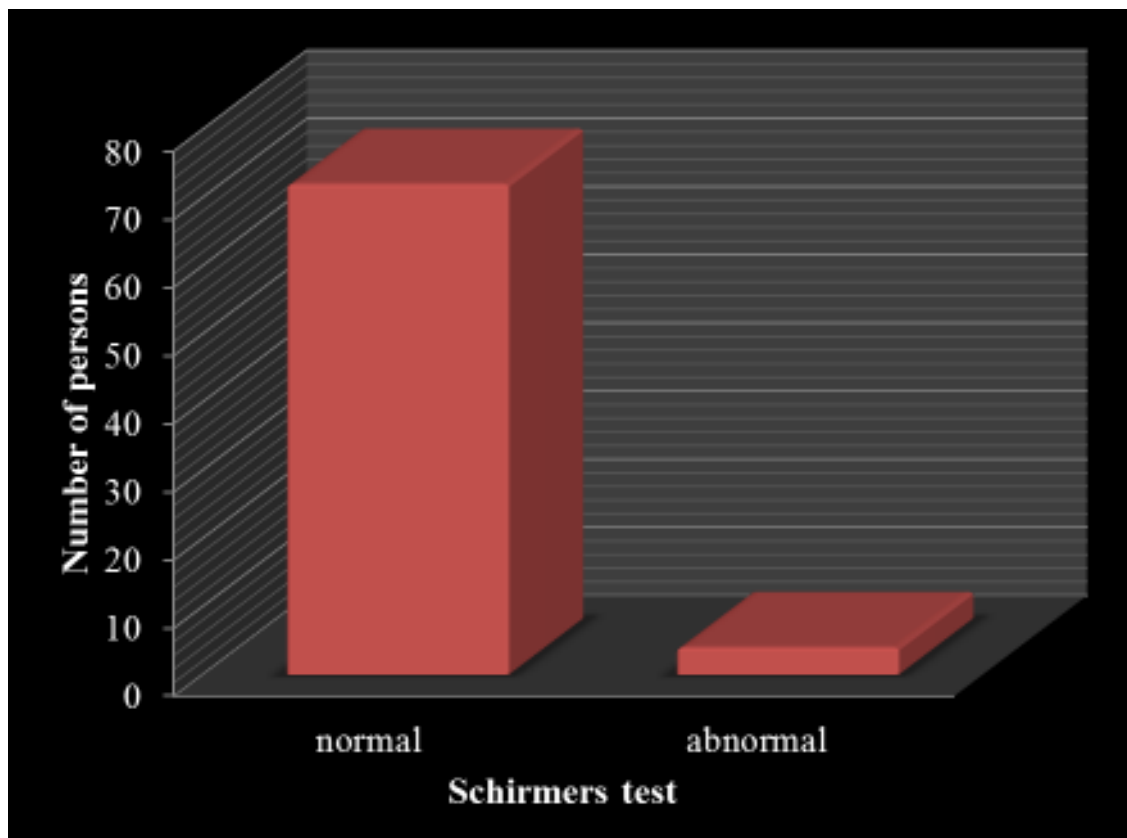
Visual fields	Without ocular manifestations	With ocular manifestations	Total
Full	46	29	75
Abnormal	0	1	1
Total	46	30	76

The chi-square value for the above table is 1.554 and the “P” value is 0.213



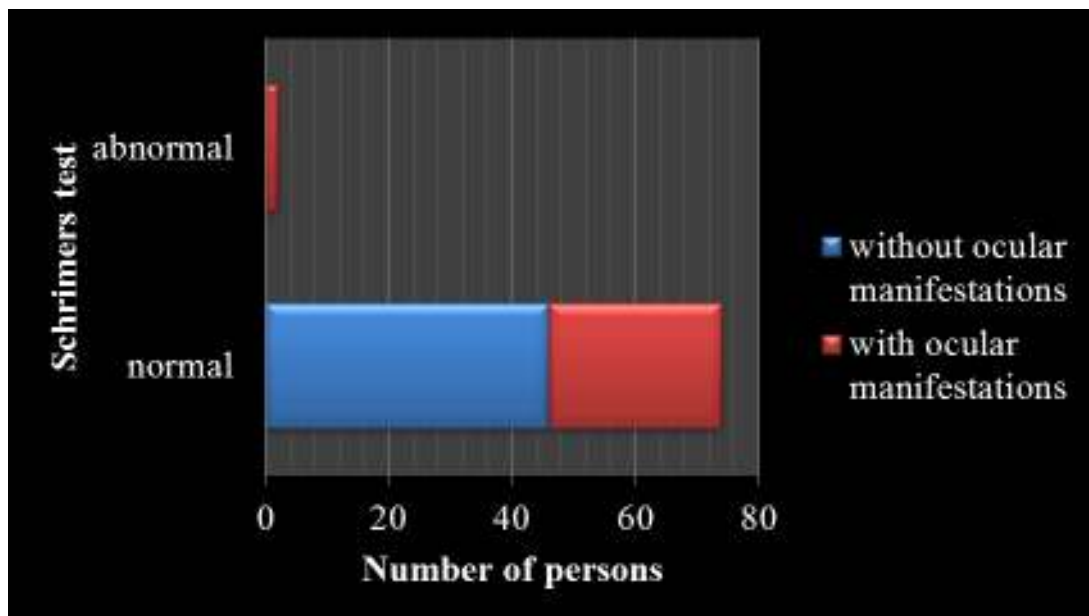
SCHIRMERS TEST:

- NORMAL: 74
- EVIDENCE OF DRY EYE PRESENT: 2



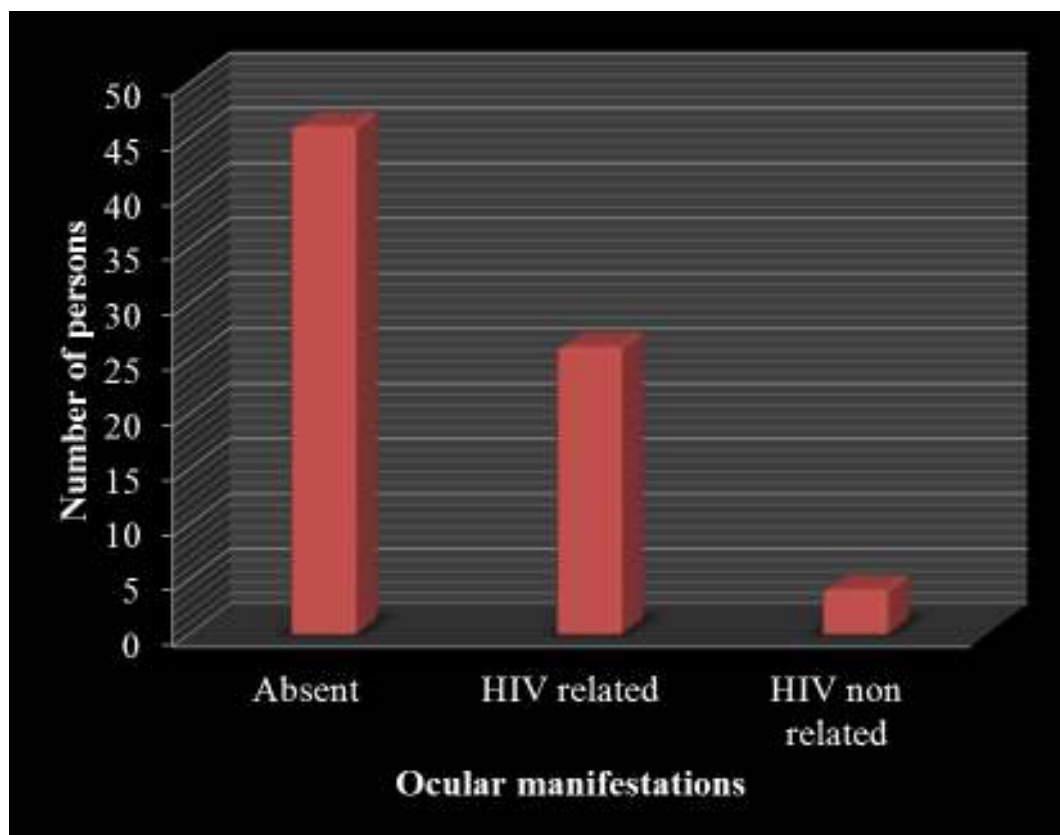
Schirmer's test	Without ocular manifestations	With ocular manifestations	Total
Normal	46	28	74
Abnormal	0	2	2
Total	46	30	76

The chi-square value for the above table is 3.150 and the “P” value is 0.076



FINAL OPHTHALMIC STATUS:

- HIV RELATED OPHTHALMIC MANIFESTATION
 - PRESENT- 26
 - ABSENT - 46
- NON HIV RELATED MANIFESTATION: 4



OCULAR MANIFESTATIONS FOUND:

I. HIV RELATED

1. POSTERIOR SEGMENT MANIFESTATIONS:

- a. HIV related retinopathy : 10 (20 eyes)
- b. Choroidal tuberculoma : 2 (2 eyes)

2. ANTERIOR SEGMENT MANIFESTATIONS:

- a. Herpes zoster ophthalmicus with Kerato uveitis :3 (3 eyes)
- b. Chronic uveitis : 1 (1 eye)
- c. Chronic keratitis: 1(1 eye)
- d. Acute anterior uveitis : 1(1 eye)

3. ADNEXAL MANIFESTATIONS:

- a. Squamous cell carcinoma of conjunctiva : 4 (4 eyes)
- b. Dry eye : 2 (4 eyes)

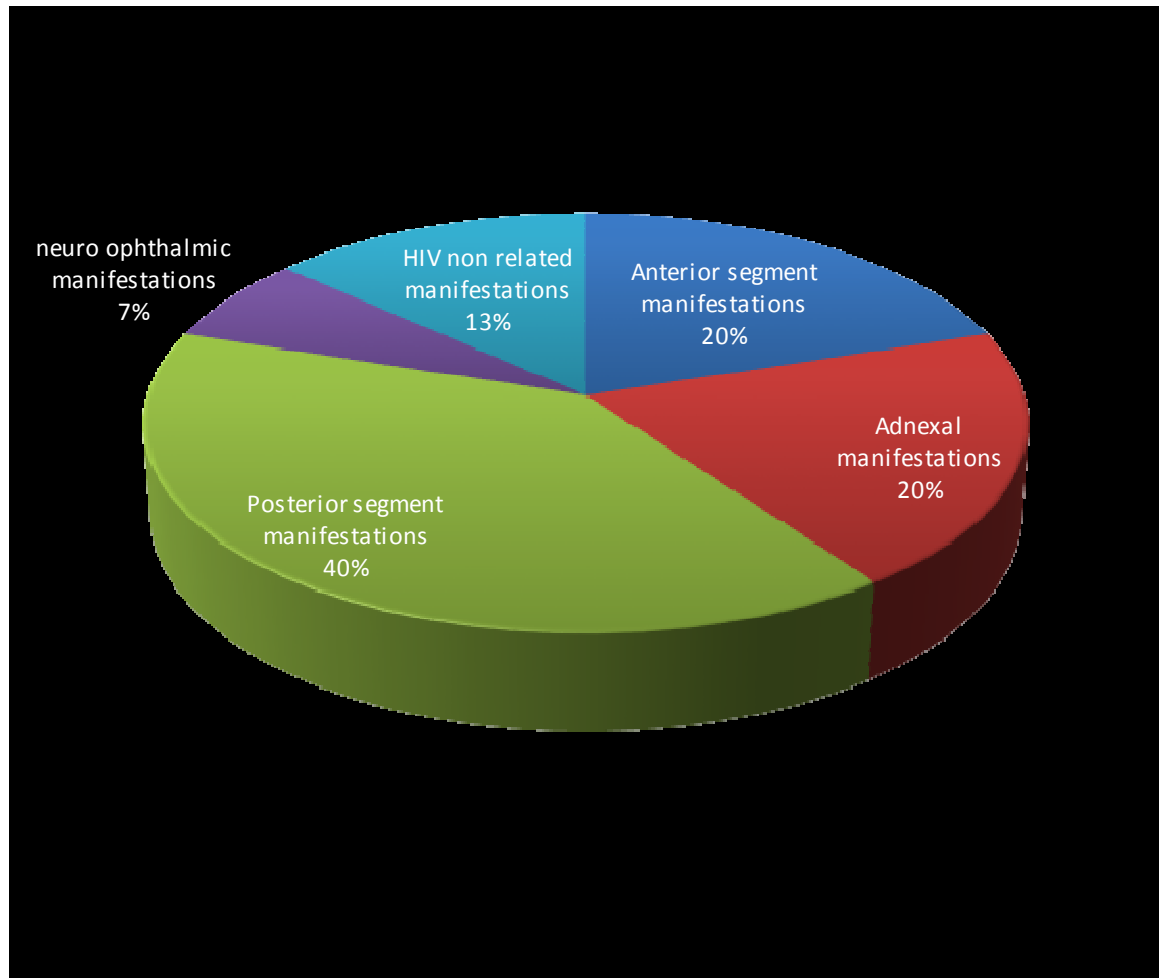
4. NEURO OPHTHALMIC MANIFESTATIONS:

- a. Chronic papilledema : 1 (2 eyes)
- b. Vertical gaze palsy : 1 (2 eyes)

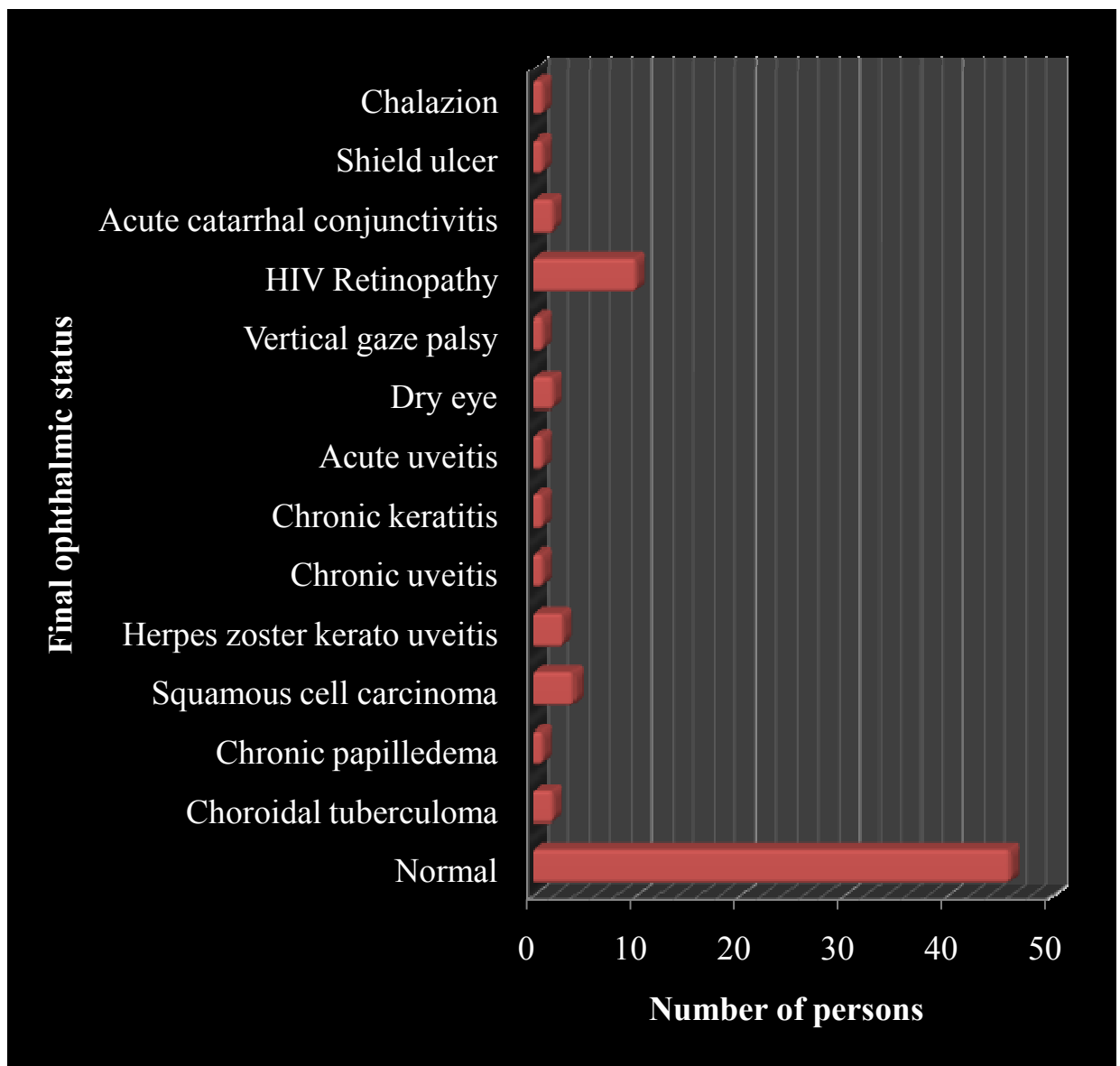
II. HIV NON RELATED

- 1. Acute catarrhal conjunctivitis : 2 (4 eyes)
- 2. Chalazion : 1(1 eye)
- 3. Shield ulcer : 1 (1 eye)

Ocular Manifestations (Total)



Final Ophthalmic diagnosis of the study group



Variable	Number of persons without ocular manifestations	Number of persons with ocular manifestations	P value
Gender			
Male:	34	19	0.326
Female:	12	11	
Age group			
< 30	7	8	0.424
31 – 40	18	9	
41 – 50	15	7	
51 – 60	6	5	
>60	0	1	
Socio economic status			
Class III	16	11	0.867
Class IV	30	19	
Marital status:			
Married	41	27	0.422
Unmarried	4	1	
Widowed	1	2	
Mode of transmission:			
Heterosexual	45	28	0.326
Homosexual	1	2	
IV drug abuse	0	0	
Blood transfusion	6	4	
Tuberculosis			
Present	45	27	0.135
Absent	1	3	
CD4 count			
< 50	1	1	0.414
51 t0 100	3	4	
101 to 150	6	3	
151 to 200	3	0	
201 to 250	3	5	
≥ 250	30	17	
Stage of the disease			
Stage 1	35	17	0.045

Stage 2	11	10	
Stage 3	0	0	
Stage 4	0	3	
Ocular symptoms:			
Nil	40	15	0.012
Defective vision	2	5	
Redness	3	3	
Irritation & FB sensation	0	4	
Photophobia	0	2	
Floaters	0	0	
Others	1	1	
Visual acuity – RE			
6/6 – 6/18	39	28	0.471
<6/18 – 6/60	6	2	
<6/60 – 3/60	0	1	
<3/60 – 1/60	0	0	
<1/60 – NO PL	0	0	
Visual acuity – LE			
6/6 – 6/18	38	26	0.276
<6/18 – 6/60	4	2	
<6/60 – 3/60	1	0	
<3/60 – 1/60	0	2	
<1/60 – NO PL	0	3	
Lids and adnexa:			
Normal	38	18	0.029
Abnormal	8	12	
Anterior segment			
Normal	43	22	0.034
Abnormal	3	8	
Posterior segment			
Normal	46	17	0.000
Abnormal	0	13	
Schirmer’s test test			
Normal	46	28	0.076
Abnormal	0	2	
Visual fields			
Full	46	29	0.213
Abnormal	0	1	

DISCUSSION

In the present study out of 152 eyes examined of 76 patients abnormal ophthalmic findings were found in 42 eyes .The abnormal ophthalmic findings which are directly related to the HIV infection were seen in 37 eyes.

PREVALANCE:

The estimated prevalence of ophthalmic manifestations associated with HIV infection at the time of diagnosis is 24.34%. The prevalence of abnormal ocular findings seen in HIV positive patients at the time of diagnosis is 27.63%.

There are many studies correlating the prevalence of Ophthalmic manifestations with HIV infection, but none were done to determine the ophthalmic status of the eye at the time of diagnosis. There is a study done by *Sophia et al* who determined the ophthalmic manifestations of HIV at the time of enrollment into ART Centre i.e. naïve to ART which proved the prevalence of ophthalmic manifestations to be 17.5%.

PROFILE OF OCULAR MANIFESTATIONS:

POSTERIOR SEGMENT MANIFESTATIONS:

In our study, the prevalence of posterior segment manifestations (n=12) were more compared to anterior segment (n=6), which exactly matches with the study done by *Sophia et al*. Among the manifestations HIV retinopathy (n=10) is most common. In the study done by *Sophia et al*, CMV retinitis is the most common manifestation followed by HIV retinopathy. This can be related to the fact that in our study the mean CD4 count was greater than 100/cu.mm as all the patients were examined at the time of diagnosis only, whereas in their study prior to enrollment in ART center screening was done. The median range of CD4 count in our study is around 300 cells/cu.mm. Two patients had evidence of ocular tuberculosis in the form of choroidal tuberculoma, who also had evidence of coexisting systemic tuberculosis. This shows the importance of systemic tuberculosis as the major opportunistic infection among HIV positive persons in India.

ANTERIOR SEGMENT MANIFESTATIONS:

The number of patients with anterior segment and adnexal ocular lesions were 16 among which 12 had HIV related ocular lesions and 4 had HIV non related ocular lesions. Among the twelve, 6 had anterior segment lesions and six had adnexal lesions.

Six patients had ocular lesions relating to cornea and uvea of which three had Herpes zoster ophthalmicus, one had chronic uveitis, one with acute iritis and one had chronic keratitis.. Hence in our study the most common anterior segment finding which was more prevalent among HIV positive persons at the time of diagnosis is Herpes zoster Ophthalmicus keratouveitis.

ADNEXAL MANIFESTATIONS:

It was surprising to note that 4 patients had squamous cell carcinoma of conjunctiva who were diagnosed as seropositive for HIV on routine testing. It shows that Squamous cell carcinoma is more prevalent than Kaposi's sarcoma in south Asian countries due to the low prevalence of human herpes virus type 8. Two patients had evidence of dry eye.

NEURO OPHTHALMIC MANIFESTATIONS:

Two patients had Neuro ophthalmological lesions which includes vertical gaze palsy and Chronic Papilledema due to tuberculous meningitis. The prevalence of Neuro ophthalmological lesions in our study is around 2.63%.

DEMOGRAPHIC PROFILE:

There was no significant association found between the patient and their demographic profile which includes age, sex, socio economic status and marital status. In the present study the prevalence of ocular manifestations in males and females among the entire study group were 25 and 14.4% respectively. While the gender specific prevalence of ocular manifestations among males and females were 36 and 47% respectively. This skewed deviation was the limitation of the study and can be attributed to the fact that the number of males who were enrolled for the study were more compared to females

Among the modes of transmission, sexual transmission by heterosexual mode was found to be more common. But there was no association found between the occurrence of ocular manifestation and mode of transmission.

CLINICAL STAGE, OCULAR SYMPTOMS, CO EXISTING HISTORY OF TUBERCULOSIS, CD4 COUNT:

Four patients had concurrent history of pulmonary tuberculosis, among which two had evidence of ocular tuberculosis. However, No association was found between both.($p=0.135$)

There was major significant association found between the clinical stage of the disease and occurrence of ocular manifestation. ($P=0.045$). Most of the patients who got enrolled for the study belonged to clinical stage I and II respectively. This shows that ocular manifestations can occur even during the initial clinical stages itself. Hence the need for ophthalmic screening at the time of diagnosis.

There was an association found between presence of ocular symptoms and the occurrence of ocular manifestations. ($P=0.012$).

In the study by *Sophia et al*, the prevalence of ophthalmic manifestations in patients with CD4 count less than 200 cells/cu.mm was 23.8%. In our study, the prevalence of ophthalmic manifestations with CD4 count less than 200/cu.mm is 10.52%. There was no association found between CD4 count and occurrence of ocular manifestations. ($P=0.414$).

OCULAR EXAMINATION AND MANIFESTATIONS:

There was significant association found between lids and adnexal examination and occurrence of ocular manifestation. ($P=0.029$). Similarly between anterior segment examination and ocular manifestation ($P=0.034$), posterior segment examination and ocular manifestation ($P=0.000$) respectively.

However, no association was found between Schrimers test and ocular manifestation ($P=0.076$) and also between visual field examination and ocular manifestation ($P=0.213$).

VISUAL IMPAIRMENT:

There was no association found between visual acuity and ocular manifestations. ($P= 0.471$ in right eye, $P=0.276$ in left eye). Among the 76 patients, 65 had normal visual acuity, 10 had visual impairment and 1 had severe visual impairment. However only 5 patients had evidence of visual impairment due to HIV related ocular manifestations. While the remaining 6 patients had preexisting ocular pathology including refractive error and cataract. Considering the visual disability, 5 patients had vision less than 3/60 in one eye other being normal (30% visual handicapped). Hence the prevalence of visual impairment due to HIV associated ocular manifestation is around 6.57%.

SUMMARY

STUDY OBJECTIVE:

1. To define the ocular manifestations of HIV/AIDS in adults at the time of diagnosis.
2. To determine the prevalence of ocular manifestations of HIV/AIDS in adults at the time of diagnosis
3. To correlate the manifestations with the demographic profile and clinical stage of the disease.
4. To determine the visual impairment associated with ocular manifestations.

STUDY DESIGN:

A Cross sectional hospital based study.

STUDY POPULATION:

A total of 76 persons who were diagnosed recently as HIV positive and attended the OP clinic of department of STD (sexually transmitted diseases) were screened for ophthalmic status with resources provided after getting a clear consent.

STUDY RESULTS:

Among the 76 persons examined 30 had ocular lesions; of which 26 had HIV related ocular manifestations and 4 had HIV non related ocular manifestation. 12 had posterior segment and 12 had anterior segment lesions, while 2 had Neuro ophthalmological lesions. HIV retinopathy is the most common isolated ocular manifestation found in about 10 persons, whereas Kerato uveitis occurred in about 6 persons and squamous cell carcinoma of conjunctiva in about 4 persons.

DISCUSSION:

Posterior segment manifestations accounts for the leading ocular manifestation as HIV retinopathy occurred in about 10 persons. There was no evidence of CMV retinitis in the study population as the mean CD4 count was above 300/cu.mm. Squamous cell carcinoma of conjunctiva occurred in 4 persons which shows the less prevalence of HHV 8 in India which causes Kaposi's sarcoma, the leading HIV related ocular neoplasm in western countries

CONCLUSION

The Ophthalmic manifestations occurring in adults due to HIV infection involve all the four groups – adnexa, anterior segment, posterior segment and Neuro ophthalmological manifestations. However, it's the posterior segment manifestations which were found to be more prevalent.

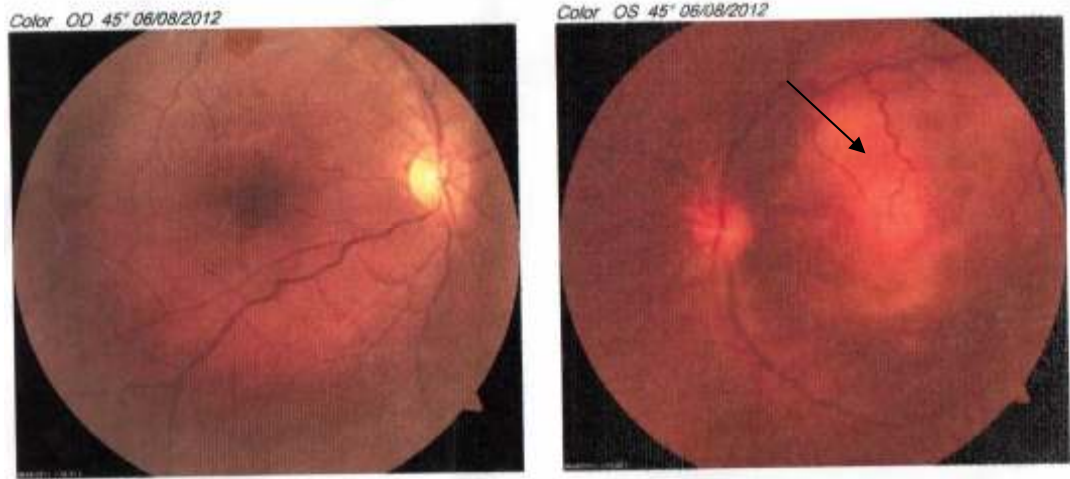
No significant association was found with the demographic profile, mode of transmission and concurrent history of tuberculosis. Though, significant association was found with clinical stage of the disease and the concomitant presence of ocular symptoms.

No evidence of opportunistic infections other than ocular tuberculosis was found as the median CD4 count was above 300/cu.mm. Also no association between ocular manifestation and CD4 count was found as most patients had CD4 count more than 300/cu.mm. This also signifies most patients were diagnosed earlier even before they develop advanced disease and less CD4 counts. However, most patients were unaware of their ophthalmic status and the need for screening which shows significant association between ocular manifestation and the screening procedures (slit lamp examination, fundus examination, and adnexal examination) in the present study.

Hence, the present study strongly emphasizes the importance of routine ophthalmic screening at the time of diagnosis of HIV seropositivity in adults.

CLINICAL PICTURES:

Choroidal tuberculoma (fundus picture)



FFA findings



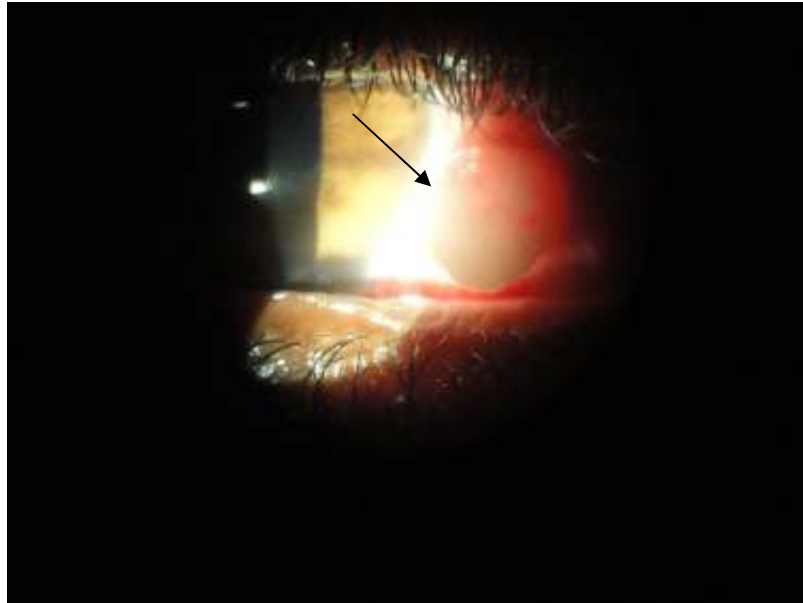
Herpes zoster Ophthalmicus:



CHRONIC KERATITIS:



SQUAMOUS CELL CARCINOMA:



After excision



HIV Retinopathy:



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PROFORMA – THESIS:

Name of the patient:

Age: sex: Occupation: Marital
status:

SES: OP no: Date of diagnosis:

CD4 count: Clinical stage of the disease:

Ocular symptoms: present/absent

Detailed history of symptoms:

History of Tuberculosis: present/absent on ATT or not

Sexual history: premarital/extra marital homosexual/heterosexual

History of IV drug abuse/blood transfusion

OCULAR EXAMINATION:

Best corrected visual acuity- right eye: left eye:

Lids and adnexal examination by torch light:

Anterior segment examination by slit lamp:

Visual fields by Bjerrum screen: RE: LE:

Schrimers test RE: LE:

Fundus examination: Direct ophthalmoscope- RE: LE:

With 90 D - RE: LE:

With indirect ophthalmoscope - RE: LE:

FINAL OPHTHALMIC STATUS:

Key to Master Chart:

MS – Marital status

MR- Married

U- Unmarried

W- Widowed

SES – Socio Economic Status

SXH – Sexual history

HT- Heterosexual

HO-Homosexual

SYMP Y/N – symptoms present/absent

IRR- irritation

RED – redness

PHB – photophobia

DV – defective vision

WAT – watering

FB- foreign body sensation

P – Pain

DIS – discharge

H- Headache

S- Swelling

TB – tuberculosis

STG – clinical stage of the disease

BT – blood transfusion

IVD – intravenous drug abuse

VA – visual acuity

RE – right eye

LE – left eye

BE – both eyes

ANT SEG – anterior segment

POS SEG – posterior segment

L & A – lids and adnexa

CCC – circum corneal congestion

CONJ – conjunctiva

CWS – cotton wool spots

VGP – vertical gaze palsy

PAP – papilledema

F – flare

C- cells

KP- keratic precipitates

HZO – herpes zoster ophthalmicus

KU- keratouveitis

SCH – Schirmer's test

D & T CV- dilated and tortuous conjunctival vessels.

HERP LES – herpetic lesions

OLD OPA – old corneal opacity

SN – solitary nodule

Q – Quadrant

ACCO – acute catarrhal conjunctivitis.

CHO TB WIT ERD – choroidal tuberculoma with exudative retinal detachment

SCC- squamous cell carcinoma.

master chart

S. N	SEX	AGE	MS	SES	REGN N	CD 4	SYMP Y/N	TB	SXH	IV D A	B T	ST G	VA	L & A	ANT SEG	POS SEG	FIELD S	SC H	FINAL
1	F	47	W	IV	S08821	136	N	NIL	HT	NIL	NIL	II	6/6 BE	N	N	BE CWS +	FULL	N	HR BE
2	F	38	Mr	IV	S08345	242	Y- IRR BE	NIL	HT	NIL	NIL	I	6/6 BE	N	N	N	FULL	DE	DRY EYE BE
3	M	39	Mr	IV	S09256	242	N	NIL	HT	NIL	NIL	I	6/6 BE	N	N	N	FULL	N	N STUDY
4	M	58	Mr	III	S08618	402	N	NIL	HT	NIL	Y	I	6/9 BE	N	N	N	FULL	N	N STUDY
5	M	29	Mr	III	S02370	509	N	NIL	HT	NIL	NIL	I	6/6 BE	N	N	N	FULL	N	N STUDY
6	F	39	Mr	IV	S08614	408	N	NIL	HT	NIL	NIL	I	6/6 BE	N	N	N	FULL	N	N STUDY
7	M	60	Mr	IV	OP N 14330	320	Y RED & PHB, DV LE	NIL	HT	NIL	Y	II	6/36 2/60	HERP LES+ CCC+	ED+ KPS+	N	FULL	N	HZV KU LE
8	M	53	Mr	IV	S N 639/12	336	Y RED & PHB LE	NIL	HT	NIL	Y	II	6/18 6/12P	HERP LES+ CCC+	EPI DEF+ KPS+ F 1+ C 1+	N	FULL	N	HZV KU LE
9	F	50	W	IV	S05636	825	N	NIL	HT	NIL	Y	I	6/6P BE	D & T CV+	N	N	FULL	N	N STUDY
10	M	55	Mr	IV	PE 112899 DIAGNSED OUTSIDE	312	Y H	NIL	HT	NIL	NIL	I	6/6P 6/9P	N	N	CWS BE +	FULL	N	HR BE
11	M	31	Mr	III	S09024	161	N	NIL	HT	NIL	NIL	I	6/6 BE	N	N	N	FULL	N	N STUDY
12	M	37	Mr	III	so8290	301	N	NIL	HT	NIL	NIL	I	6/9 BE	N	N	N	FULL	N	N STUDY
13	M	45	Mr	III	S06153	164	N	NIL	HT	NIL	NIL	I	6/6 BE	N	N	N	FULL	N	N STUDY
14	M	33	Mr	IV	S07626	423	N	NIL	HT	NIL	NIL	I	6/6 BE	N	N	N	FULL	N	N STUDY

15	F	70	W	IV	S09092	854	Y - DV, RED, PHB LE	NIL	HT	NIL	Y	II	6/12 HM+	CCC+ HERP LES+	EPI DEF+ F 2+ C 2+	N	RE FULL LE CBT	N	HZV KU LE
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16	F	46	Mr	III	S08254	285	N	NIL	HT	NIL	NIL	I	6/6 BE	N	N	N	FULL	N	N STUDY
17	F	36	Mr	III	S08961	55	N	POSITIVE ON ATT	HT	NIL	NIL	IV	6/6 BE	BITOT SPOTS+	N	SN ST Q LE	FULL	N	CHO TB LE
18	M	36	Mr	III	S09077	280	DV LE	NIL	HT	NIL	NIL	I	6/36 HM+	CCC+	EPI DEF+	N	RE FULL LE CBT	N	SHIELD ULCER LE
19	M	56	Mr	IV	S08564	212	RED P W LE	NIL	HT	NIL	NIL	I	6/9 6/6P	PAPILLAE+	N	N	FULL	N	N STUDY
20	F	30	Mr	IV	S08959	47	N	NIL	HT	NIL	NIL	I	6/9P 6/9	N	N	CWS BE +	FULL	N	HR BE
21	M	39	Mr	III	S08940	300	N	NIL	HT	NIL	NIL	I	6/6 BE	D & T CV	N	N	FULL	N	N STUDY
22	M	52	Mr	IV	S03613	237	N	NIL	HT	NIL	NIL	II	6/12 6/18	N	N	CWS BE+	FULL	N	HR BE
23	M	38	Mr	III	S08824	253	N	NIL	HT	NIL	NIL	I	6/6P 6/6	D & T CV+	N	N	FULL	N	N STUDY
24	M	36	Mr	III	S08934	145	N	NIL	HT	NIL	NIL	I	6/6 BE	N	N	N	FULL	N	N STUDY
25	M	33	Mr	III	S08929	270	N	NIL	HT	NIL	NIL	II	6/6 BE	N	N	N	FULL	N	N STUDY
26	F	34	Mr	IV	S07613	330	N	NIL	HT	NIL	NIL	II	6/6 BE	N	N	N	FULL	N	N STUDY
27	F	33	Mr	IV	S05636	210	N	NIL	HT	NIL'	NIL	I	6/9P 6/6	N	N	N	FULL	N	N STUDY
28	M	30	Mr	IV	S08909	87	N	NIL	HT	NIL	NIL	II	6/24P BE	N	N	N	FULL	N	N STUDY
29	M	50	Mr	IV	S08925	120	N	NIL	HT	NIL	Y	II	6/60 4/60	N	N	N	FULL	N	N STUDY
30	M	37	Mr	IV	S08567	87	DV LE	NIL	HT	NIL	NIL	II	6/6 BE	N	N	N	FULL	N	N STUDY
31	M	29	Mr	IV	S07666	286	N	NIL	HO	NIL	NIL	I	6/6 BE	N	N	N	FULL	N	N STUDY
32	M	57	Mr	IV	S08946	49	N	NIL	HT	NIL	NIL	I	6/12	N	N	N	FULL	N	N STUDY

													6/6						
33	F	26	U	IV	S05935	285	N	NIL	HT	NIL	NIL	II	6/6 BE	N	N	N	FULL	N	N STUDY
34	M	50	Mr	IV	S08847	141	N	NIL	HT	NIL	NIL	I	6/36 6/18	N	N	N	FULL	N	N STUDY
35	M	41	Mr	IV	S07852	532	N	NIL	HT	NIL	NIL	I	6/6 BE	N	N	N	FULL	N	N STUDY
36	F	30	Mr	III	S06150	331	N	NIL	HO	NIL	NIL	I	6/6 BE	N	N	CWS BE +	FULL	N	HR BE
37	M	48	Mr	III	S08840	82	Y DV PHB LE	NIL	HT	NIL	NIL	II	6/18 6/36	CCC+	EPI DEF+ F2+ C2+	N	FULL	N	CHR KER LE
38	M	45	Mr	IV	S08757	457	N	NIL	HT	NIL	NIL	I	6/6 BE	N	OLD OPA IQ+	N	FULL	N	N STUDY
39	F	47	Mr	IV	S08897	226	N	NIL	HT	NIL	NIL	I	6/12 6/24	N	N	N	FULL	N	N STUDY
40	M	43	Mr	IV	OP N 15444	102	RED PHB DV LE	NIL	HO	NIL	NIL	II	6/24 1/60	CCC+	OLD KPS+ PS+	N	RE FULL LE CBT	N	CHR UVE LE
41	F	22	U	III	S08692	317	N	NIL	HT	NIL	Y	I	6/6 BE	N	N	N	FULL	N	N STUDY
42	M	45	Mr	III	S09227	79	H	POSITIVE ON ATT	HT	NIL	NIL	IV	6/9 6/6	N	N	DE BE+,	EBS BE+	N	CHR PAP BE
43	M	39	Mr	IV	S03557	85	DV P PHB LE	POSITIVE ON ATT	HT	NIL	NIL	IV	6/6 HM+	CCC+	OLD KPS+ PS+	EG IN ST Q WITH E RD IN LE+	RE FULL LE CBT	N	CHO TB WITH ERD LE
44	M	47	Mr	IV	S08923	402	RED DIS RE	POSITIVE ON ATT	HT	NIL	NIL	I	6/9 6/12	CONJ CONGESTION+	N	N	FULL	N	ACCO BE
45	F	21	U	IV	S01415	451	IRR FB BE	NIL	HT	NIL	NIL	I	6/6 BE	N	N	N	FULL	DE	DRY EYE BE
46	F	27	Mr	IV	S05108	252	N	NIL	HT	NIL	NIL	I	6/6 BE	N	N	CWS BE+	FULL	N	HR BE
47	M	40	Mr	IV	S01925	140	N	NIL	HT	NIL	NIL	I	6/6 BE	N	N	N	FULL	N	VGP BE
48	M	47	Mr	IV	S09341	452	N	NIL	HT	NIL	NIL	I	6/6 BE	N	N	CWS	FULL	N	HR BE

																BE+			
49	F	34	Mr	III	S08412	312	P RED BE	NIL	HT	NIL	NIL	I	6/18 6/36	CONJ COGESTION+	N	N	FULL	N	ACCO BE
50	M	40	Mr	IV	S06991	620	N	NIL	HT	NIL	NIL	I	6/12 6/9	N	N	N	FULL	N	N STUDY
51	M	32	Mr	III	OP N 01891	381	N	NIL	HT	NIL	NIL	I	6/6 6/12	N	N	N	FULL	N	N STUDY
52	M	47	Mr	IV	S08866	97	N	NIL	HT	NIL	NIL	II	6/6 BE	N	N	N	FULL	N	N STUDY
53	M	35	Mr	III	S02278	327	S LE	NIL	HT	NIL	NIL	I	6/6 6/12	CHALAZION LE	N	N	FULL	N	CHALAZION LE
54	F	42	Mr	IV	S07957	302	N	NIL	HT	NIL	NIL	I	6/9 6/9	N	N	N	FULL	N	N STUDY
55	M	38	Mr	III	OP N 6124	920	IRR RED LE	NIL	HT	NIL	NIL	I	6/18 BE	RAISED CONJ LES+ LE	N	N	FULL	N	SCC LE
56	F	31	Mr	III	S01068	381	RED P PHB LE	NIL	HT	NIL	NIL	I	6/6 6/12	CCC+	KPS+ C1+ F1+	N	FULL	N	AC IRI LE
57	M	45	Mr	IV	OP N 6493	285	IRR RED LE	NIL	HT	NIL	NIL	II	6/6P BE	RAISED CONJ LES+ RE	N	N	FULL	N	SCC RE
58	M	42	Mr	IV	S06410	400	N	NIL	HT	NIL	NIL	I	6/18 6/9	N	N	N	FULL	N	N STUDY
59	F	36	Mr	III	S08492	168	N	NIL	HT	NIL	NIL	I	6/6 BE	N	N	N	FULL	N	N STUDY
60	M	55	Mr	IV	S08750	121	N	NIL	HT	NIL	Y	II	6/6 BE	N	N	N	FULL	N	N STUDY
61	M	48	Mr	IV	P 3749 (DIAGNSED OUTSIDE)	341	N	NIL	HT	NIL	NIL	II	6/18 6/12	N	OLD OPA IQ RE+	N	FULL	N	N STUDY
62	F	40	Mr	IV	S09302	282	N	NIL	HT	NIL	NIL	I	6/9 6/9	N	N	N	FULL	N	N STUDY
63	M	25	U	III	S09301	133	N	NIL	HT	NIL	NIL	II	6/6 BE	N	N	N	FULL	N	N STUDY
64	M	46	Mr	IV	S09299	108	N	NIL	HT	NIL	NIL	II	6/9 BE	N	N	N	FULL	N	N STUDY
65	M	40	Mr	IV	S09724	620	N	NIL	HT	NIL	NIL	I	6/12 6/9P	N	N	N	FULL	N	N STUDY
66	F	56	Mr	IV	S09231	328	N	NIL	HT	NIL	Y	I	6/24 BE	N	N	N	FULL	N	N STUDY

67	M	60	Mr	IV	S09041	412	N	NIL	HT	NIL	Y	I	6/36 BE	N	N	N	FULL	N	N STUDY
68	M	58	Mr	IV	S09349	402	N	NIL	HT	NIL	NIL	I	6/12 BE	N	N	N	FULL	N	N STUDY
69	F	25	Mr	III	S07404	205	N	NIL	HT	NIL	NIL	II	6/9 BE	N	N	CWS BE +	FULL	N	HR BE
70	M	24	Mr	III	S08232	215	N	NIL	HT	NIL	NIL	I	6/6 BE	N	N	CWS BE+	FULL	N	HR BE
71	M	25	U	III	S09198	401	N	NIL	HT	NIL	NIL	I	6/6 BE	N	N	N	FULL	N	N STUDY
72	M	30	Mr	IV	S08450	414	N	NIL	HT	NIL	NIL	I	6/6 BE	N	N	N	FULL	N	N STUDY
73	M	44	Mr	IV	S06335	321	N	NIL	HT	NIL	NIL	I	6/24 BE	N	N	N	FULL	N	N STUDY
74	M	28	Mr	III	S09352	302	N	NIL	HT	NIL	NIL	I	6/6 BE	N	N	CWS BE+	FULL	N	HR BE
75	M	50	Mr	IV	S06734	312	RED IRR RE	NIL	HT	NIL	NIL	II	6/12 6/9	RAISED LES CONJ RE+	N	N	FULL	N	SCC RE
76	M	40	Mr	IV	S07532	345	IRR RED RE	NIL	HT	NIL	NIL	I	6/9 BE	RAISED LES CONJ+ LE	N	N	FULL	N	SCC LE